James A Reeman

The New England Journal of Medicine

Formerly
The Boston Medical and Surgical Journal
Established 1828

Volume 232 FEBRUARY 1, 1945 Number 5

THE USE OF THE TERM "PSYCHONEUROSIS" 121
Jackson M. Thomas

QUANTITATIVE SEROLOGIC TESTS FOR SYPHILIS 124
Albert Heyman

CHRONIC MONARTICULAR ARTHRITIS 128
John G. Kuhns

THE EFFECT OF PENICILLIN ON INOCULATION MALARIA 133
J. A. Hindle, A. S. Rose, L. D. Trevett, and C. Prout

MEDICAL PROGRESS: ORTHOPEDIC SURGERY: THE PROBLEM OF THE INTERVERTEBRAL DISK 137
Carroll B. Larson

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL 140

EDITORIALS
Standards of Medical Education 146
A New and Rapid Laboratory Test for Smallpox 147

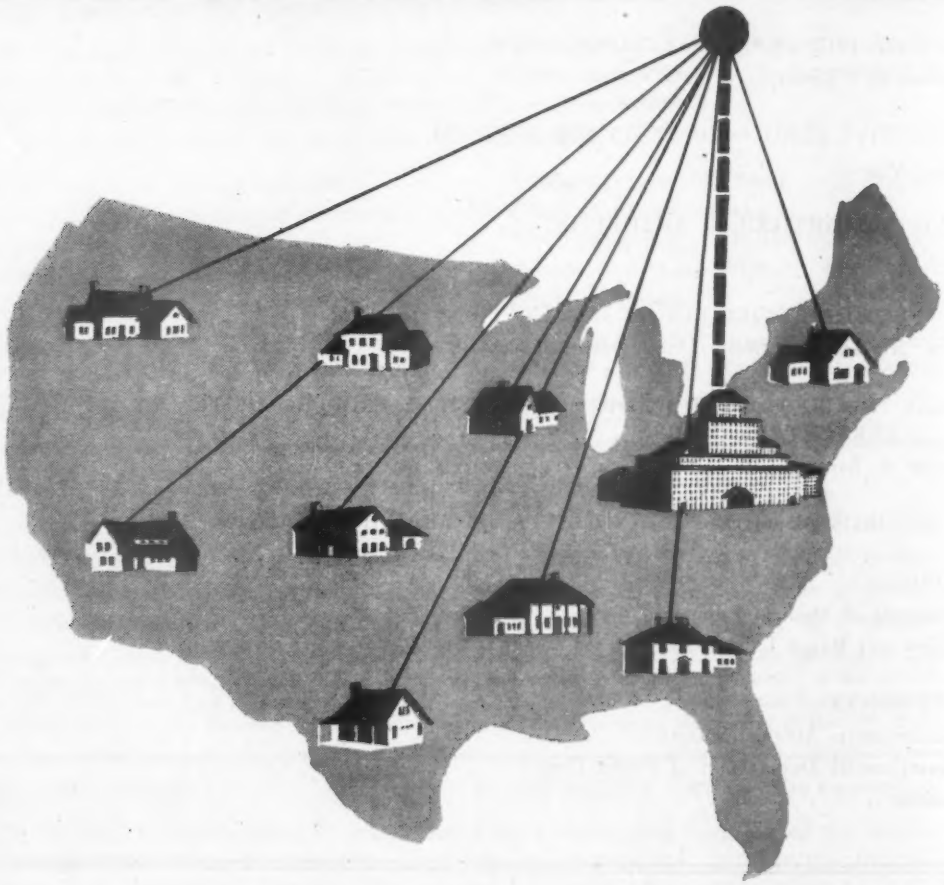
DEPARTMENTS
Massachusetts Medical Society 147
Massachusetts Department of Public Health 148
Notices 148

Owned and Published by the Massachusetts Medical Society

Published weekly at 8 Fenway, Boston 15, Massachusetts.
Domestic, $6 per year, 25c per copy (medical students, $3.50 per year); Canada, $7.04 (Boston funds); foreign, $8.52.
Entered as second-class matter November 16, 1932, at the post office at Boston, Massachusetts, under the Act of March 3, 1879.

Copyright, 1945, by the Massachusetts Medical Society.

9 out of 10 cases of EPILEPSY are treated in the home



The New England
Journal of Medicine

Copyright, 1945, by the Massachusetts Medical Society

Volume 232 FEBRUARY 1, 1945 Number 5

THE USE OF THE TERM "PSYCHONEUROSIS"

LIEUTENANT COLONEL JACKSON M. THOMAS, M.C., A.U.S.*

MANY men and women discharged from the Army for medical reasons have been classified as neuropsychiatric cases. This fact and the trend of statistics in medical journals, newspapers and magazines pertaining to war neuroses suggest that it would be unfashionable today not to show alarm at the rate soldiers are developing nervous disorders. History discloses, however, that there is a similarity between the widespread concern over the conditions generally described as psychoneuroses and the ill-founded apprehension voiced by Beard[1] in 1881, when he declared:

> All this is modern and originally American; and no age, no country and no form of civilization, not Greece, nor Rome, nor Spain, nor the Netherlands, in the days of their glory, possessed such maladies. Of all the facts of modern sociology this rise and growth of functional nervous disease is one of the most stupendous, complex and suggestive.

These words refer to conditions that Beard included under the appellations "nervous exhaustion," "neurasthenia" and "American nervousness" — terms that, like Charcot's "*grande hystérie*" and Morton Prince's "multiple personality," cause a false alarm in psychiatric circles similar to that felt by some psychiatrists with reference to psychoneurosis. That many American soldiers have been judged to be victims of this malady and that the facilities of the Veterans Administration are being organized to care for numbers of neuropsychiatric cases are a matter of record and tend to make it difficult to believe that the wolf of psychoneurosis is not at the door this time. On the other hand, if the manifold conditions under which this war is being waged are borne in mind, it seems reasonable to ask what normal reactions under these ordeals might be. Alternating between battling a cunning and skilful enemy and contending with long periods of idleness, homesickness and boredom in the cold of the Arctic, in the heat and disease of the tropics and in the dust of the desert puts every man's emotions under a strain. Add to these factors delays in the delivery of mail or, still worse, the arrival of letters and hometown newspapers in which the soldier is told that the people back home are continuing to motor to Florida in the winter and to the Berkshires in the summer, and the soldier may be granted a variety of emotional reactions in his foxhole. Some of these will be psychoneurotic and others psychotic in nature, for experience has shown that in any large organization of men a certain percentage inevitably manifest mental disorder. Others, however, will be mere responses to the situation — unlinked to unconscious factors to which one is accustomed to attribute the symptoms of functional nervous disorder.

From a psychopathologic point of view, the psychoses that I have seen in this war have not differed from those observed in a busy psychopathic hospital in peacetime, except in the subject matter of the delusions and hallucinations, which vary, as they have throughout the ages, with the contemporary topics of preoccupation. This statement holds true for that group of cases regarded as acute schizophrenias, which some psychiatrists think are peculiar to this war. These cases, characterized by short periods of confusion, transitory delusions and hallucinations and quick recovery soon after admission to a hospital, are closely similar to the clinical states of emotional turmoil to which Campbell[2] often called attention. They vary from the latter only in that the subject matter of their pathologic beliefs is more often concerned with factors prevalent in a man's thoughts in time of war. The way the patient deals with these factors, however, in war or peace, depends on the same mental mechanisms that the normal mind utilizes in adapting itself to any condition of stress.

The practical disposition of psychoses in the Army is clear-cut. Experience has shown that the majority of these patients should be discharged from the service. Some of the psychoses instigated by infective and exhaustive states, which clear up when the organic, debilitating processes subside, are exceptions to this general policy.

A widespread misuse of the term "psychoneurosis" in the present war has made the treatment and disposition of cases placed in this diagnostic classification more complex than that of the psychoses. Some of the difficulty is due to the fact that the psychiatrist is too often unfamiliar with the life of

*Associate in psychiatry, Harvard Medical School, and superintendent, Channing Sanitarium, Wellesley, Massachusetts (on leave of absence).

a soldier in the field. Imbued with theories of abnormal human behavior, remaining within the wards of a hospital and feeling the necessity to fit every record into the prevailing order of a psychiatric system, he runs the risk of confusing signs of boredom, homesickness, reactions against discipline and the normal apprehension that many excellent soldiers experience before going into battle with symptoms of a true psychoneurosis. The borderline between normal reactions to difficult situations and emotional states that are to be regarded as symptoms of an ominous personality disorder is sometimes a narrow one. Human nature is not a standardized affair. Normal men differ in their output of energy and in their medium of self-expression. Some are more sensitive than others in dealing with their diverse inner needs and with the complex demands of military life.

The discussion of issues involved in some of the equivocal states of mind attributed to psychoneurotic mechanisms in this war may be clarified if attention is focused on concrete case histories. To this end I shall confine myself to descriptions of cases that I have examined.

CASE 1. A 34-year-old, married private first class, the father of two children, enlisted in the Air Force on September 23, 1942. His childhood had been normal. After completing high school, he attended a business college for 2 years. Thereafter he worked efficiently for 14 years for an electrical company. During that time his health was good. Soon after he enlisted in the Air Force he was assigned to the ground crew of a bomber squadron, with which unit he went to Africa in February, 1943. Early in May of the same year he spent a week in a field hospital because of an unexplained fever. When he returned to his unit, he was assigned to security guard duty at a post in advance of the airfield, to aid in protecting it against surprise attacks by the enemy. In the latter part of that month he began to be troubled by insomnia, anxiousness, spells of crying and "the jitters." He grew melancholy, feared he would never live to see his wife and children again, and deplored the fact that he had enlisted in the service. Thoughts of his family were intensified when he was cautioned to be more on the alert than usual, as a result of a rumor that enemy paratroopers had descended in the proximity of his post. The "jitters" increased, but he continued to perform his duty until July 23. On that date he reported to his unit medical officer, who at once sent him to a hospital in Egypt, where a diagnosis of psychoneurosis, anxiety state, was made. He was given Sodium Amytal and kept asleep almost continuously for 2 days. He improved but continued to be nervous and was evacuated to a general hospital some distance from the combat area. On November 11, he reached a hospital in the United States. En route home most of his symptoms disappeared. By December 7 all his symptoms had disappeared. He slept well, did not cry once after setting foot on American soil, was free of the "jitters," and asked to be returned to duty. Questioning disclosed that he had a good understanding of the problems that had troubled him in Africa. He was returned to duty with a diagnosis of simple adult maladjustment.

It is significant that this patient's internal equilibrium was not upset before he entered the Army, nor thereafter until he found himself in the proximity of dangerous combat. Confronted by death and tortured by images of his wife and children on the one hand, and prodded by a sense of duty to his country on the other, he developed the "jitters," cried and could not sleep. Such a reaction incapacitated him at the time, but I doubt that one would have had to peer into the depths of his unconscious to see that his conflict represented no more than a struggle between an urge for self-preservation and a sense of duty.

CASE 2. A 27-year-old, unmarried sergeant entered a general hospital in England in May, 1943, because of a respiratory infection. He had been inducted into the Army in June, 1942, and soon thereafter was assigned to an organization of engineers, with which he arrived in England in February, 1943. His record in the Army was good. Until the time he entered the hospital he had never consulted a medical officer. His respiratory condition disappeared, but in the course of the usual questions pertaining to his medical history, he stated that he sometimes vomited soon after meals. This information led to a complete gastrointestinal study, which disclosed no structural disease. The case was referred to a psychiatrist, who made a diagnosis of gastric neurosis and recommended transfer to a neuropsychiatric hospital. This recommendation was carried out. In that hospital the patient reiterated that he sometimes vomited after meals but added that he was not concerned about the matter since he had occasionally vomited small amounts of food for 2 years before he entered the Army. He was puzzled, however, over the fact that he was regarded as neurotic, and volunteered that he never would have told the medical officer in the first hospital that he vomited if he had known that by doing so he would be sent to a psychopathic hospital. He stated that before he entered the Army he drove a large van regularly over a distance of 500 miles. Along the route he stopped for meals at roadside houses. If he continued his trip immediately after eating, when he had previously driven a long distance, he sometimes found it necessary to get out of the van and vomit part of what he had eaten. Having done so, he continued his trip without further discomfort. According to his statements, this was such a recognized and frequent happening with other drivers that the company physician who examined all drivers every 6 months questioned them specifically about it.

In England, the patient was an efficient driver of a bulldozer tractor. He occasionally regurgitated small amounts of food if he worked hard soon after eating, but he was not concerned about this any more than he had been before his induction, accepting it as peculiar to the type of work he performed. There was no loss of weight. After 3 weeks' observation, during which time the patient regurgitated a small amount of food on only one occasion after breakfast, a diagnosis of no disease was made and he was granted his wish to return to duty.

This case illustrates how a simple vegetative habit, a condition that may have been instigated by the nature of a patient's work, is sometimes thought to be an expression of a psychoneurotic type of conflict of emotions. On the contrary, this patient showed no concern about his gastrointestinal tract. He adapted himself well to civilian life and to the Army. It is unlikely that he would have come to the attention of medical officers but for his respiratory infection.

CASE 3. A 29-year-old, married corporal, a mechanic, participated in the invasion of Sicily. His early development was normal. After completing the 7th grade at school he worked at various jobs, finally securing a night position with an express company, which he held at the time he entered the Army. He married at 22 a girl whom he had impregnated. Their marriage was an unhappy one, owing to the wife's not showing the proper interest in the child and having illicit sex relations with other men. The patient was inducted into the Army in May, 1941. Soon after he completed his basic training he was assigned to an Ordnance organization as a mechanic. He showed no signs of nervousness before entering the Army, nor thereafter did he come to the attention of medical officers until July 10, 1943, when he took part in

the invasion of Sicily. On that occasion, as his unit debarked from barges, German artillery and dive bombers opened up with devastating effect and continued to harass the invaders throughout the day. One of the patient's friends was wounded. Fear for his own safety increased. When a bomb fell in a bivouac area and killed many soldiers, he lost control, ran back and forth on the beach, and cried out with terror. This behavior caused him to be admitted to an emergency hospital, where he remained for only a few days. He then rejoined his unit, with which he continued to do duty until the end of July, when trembling, fear, uncontrollable crying and a lack of desire for food led medical officers to evacuate him by airplane to a station hospital in Africa on July 30. Five days later he was sent to duty at a replacement pool. He soon became emotionally disturbed again and was sent to another station hospital, whence he was evacuated to the United States with a diagnosis of psychoneurosis, anxiety state. By the time he had reached a general hospital in this country on November 21, all his symptoms had disappeared. He slept well, showed no signs of anxiety, and attributed his emotional disturbance in Sicily to an inability to withstand combat conditions. He asked to be permitted to return to duty elsewhere as a mechanic, "to regain my self-respect." On December 11, a board of medical officers diagnosed his case as one of simple adult maladjustment and recommended that he be returned to duty other than combat. This recommendation was carried out, and so far as is known he is adjusting well.

The state of mind that this soldier manifested under fire is another example of the emotional turmoil that some men undergo as the result of a conflict between a fear of death and a sense of duty. Although trembling, crying and apprehension persisted after he was removed from the combat area, such was the case only so long as there was likelihood that he would re-enter it.

Case 4. A 20-year-old, unmarried private in the Field Artillery participated in the invasion of Italy. As in Cases 1 and 3, he had no neuropsychiatric record until the time he entered a combat zone. On September 14, 1943, he was admitted to an evacuation hospital, where a diagnosis of psychoneurosis, anxiety state, severe and manifested by extreme tremulousness, fear and panic reaction, caused by combat, was made. Two days later he was transferred to a station hospital. There he was described as a very shaky, wildly staring, immature, 20-year-old boy with only 7 months' service in the Army. In the early phase of the invasion, German 88's shelled his unit's gun emplacements and during that time the patient was in a constant state of panic; he spent all his time in a foxhole. He could not recall the events of a period of 3 days. He appeared to be "frozen with fright," and whenever he heard a plane he shook violently. The diagnosis of psychoneurosis, anxiety state, was confirmed, and the patient was evacuated to a general hospital in the United States, arriving there on November 21, by which time his symptoms had disappeared. Soon after admission he stated that he felt as well as ever and expressed a desire to return to duty. Later, however, after a furlough to his home, he insisted that he should not be returned to duty because he thought that some of the symptoms he had shown in Italy would return. His attitude indicated a letdown in morale more than it pointed to a persistence of the symptoms for which he had been removed from the combat zone. He was sent to duty in the United States with a diagnosis of simple adult maladjustment.

Discussion

The cases that have been described are samples of the emotional states under discussion that are frequently classified with the psychoneuroses. That there are many genuine psychoneuroses detected in the Army for the first time overseas is beyond argument. If, however, one is to retain the generally accepted concept that a psychoneurosis is a nervous disorder dependent on complicated mechanisms of the mind involving unconscious conflicts, it is difficult to reconcile the reactions exemplified by the case histories cited with this condition. The fear, fright and tremulousness shown in Cases 1, 3 and 4 constitute a behavior pattern that has been witnessed in armies throughout the ages. Until the advent of modern psychiatry, such conduct was attributed to a variation in men's capacity to sever themselves from their usual way of life and to conquer a fear of impending death. The will to fight, morale, training, fatigue, disheartening reverses and leadership were recognized as factors able to influence a man's emotions. These factors are acknowledged in this war, but the frequency with which the diagnosis of a psychoneurosis is made raises a suspicion that psychiatrists have encouraged a shrouding of them in an ill use of terminology. In doing so they have thrown the problem of psychoneurosis out of focus with what seems to be the facts. The prompt recovery of many patients when they are removed from a difficult situation adds weight to this assumption.

I saw patients in England, members of the Air Force, who were in combat over the Continent and others who had not been in combat, and considered them unsuitable for further duty. They were returned to the United States with a diagnosis of psychoneurosis. Before they arrived, I was ordered to report for duty at the same hospital to which they were later admitted. Re-examination of some of these patients disclosed that a remarkable improvement had taken place in them, especially in those who had not been in combat. This observation opened my eyes wider to the haste that I had been guilty of in the use of the term "psychoneurosis." In some cases I had mistaken boredom, homesickness and what the British call "morale lesions" for symptoms of a nervous disorder.

Recent use of the word "anxiety" illustrates further how muddled is the present knowledge of the psychoneuroses. There are psychiatrists who regard the familiar fear of a soldier in a dangerous situation as a measure of the emotion of an anxiety neurosis. This is tantamount to calling all frightened and bewildered soldiers psychoneurotic. There was a time when "anxiety" was considered an appropriate word for the emotion present in clinical states characterized by palpitation, dyspnea, sweating, anxiousness and apprehension. Of late, however, this word has been used so loosely that it has almost acquired buoyant and ethereal qualities. This careless use of the term does injustice to the Army, the soldier and the taxpayer. So does the term "depression" when it is applied to simple nostalgias. These latter conditions were often seen in World War I. When the cause, which was absence from home or some factor related to it, was removed, the patient promptly recovered. Salmon[3] cited cases who recovered on the voyage home, some

doing this so rapidly that a suspicion of malingering arose. Similar recoveries are being seen in the present war. They should allay the fears entertained with regard to some of the erroneously classified psychoneuroses.

It may be argued that a disappearance of anxiety and insomnia under the conditions cited does not constitute a cure, and that the unconscious must be exposed to remove the real trouble. This point of view may be correct for some true psychoneuroses. The tension and anxiety of the cases discussed here, however, seem to have arisen from obviously trying situations rather than from hidden conflicts.

If the reactions under discussion are to be excluded from the psychoneurotic group, it is in order to ask what name is to be given them. The idea that an emotionally upset soldier is not a particular example of a recognized disorder is disturbing to some psychiatrists. Nor does modern warfare permit the outlet that Joshua seems to have had before the siege of Jericho, when it was directed that "the fearful and faint-hearted return unto his home lest his brethren's heart faint as well as his heart."

No one who is familiar with the fleeting fashions in psychiatric nomenclature wants to be caught adding another term to the confusion. Moreover, it is obvious from what has been said that I believe that some of these cases present problems in morale, discipline and stamina. If this is so, it follows that any term connoting a mental disorder will cloud the issue. The answer to the question seems to rest in the prophylactic orientation program now under way — the prevention of states that require a stigmatizing name.

For the patients who reach a hospital, regulations permit the use of the terms "observation — no disease found" and "simple adult maladjustment." The latter term does not always fit the picture, but for the patient returning to duty it is less of a handicap when he reaches his unit or a replacement pool than the term "psychoneurosis."

References

1. Beard, G. M. *American Nervousness: Its causes and consequences.* A supplement to *Nervous Exhaustion (Neurasthenia).* New York: G. P. Putnam's Sons, 1881. P. 7.
2. Campbell, C. M. *Destiny and Disease in Mental Disorders.* 207 pp. New York: W. W. Norton & Company, Inc., 1935.
3. Salmon, T. W. Unpublished data.

QUANTITATIVE SEROLOGIC TESTS FOR SYPHILIS*

ALBERT HEYMAN, M.D.†

ATLANTA, GEORGIA

QUANTITATIVE serologic tests for syphilis have become more widely used in recent years following the introduction of intensive methods of syphilotherapy. These tests not only are useful in methods of rapid treatment but are often of considerable value in the management of various problems encountered in the diagnosis of syphilis.[1,2] It is the purpose of this report to discuss the indications for quantitative serologic testing and to illustrate how these tests, when used judiciously, may aid greatly in the recognition of certain manifestations occurring in syphilitic infection.

The quantitative titer of syphilitic serum may be determined by several methods. The smallest amount of antigen required for a positive reaction can be measured, the least amount of complement necessary to produce fixation can be determined or, finally, the serum can be diluted until it ceases to give a positive reaction.[3] The last-named technic is the one most widely used and is the method employed in our laboratory. The serologic reaction is performed with serial dilutions of serum, the reagin titer being the highest dilution of serum giving a positive result. Thus, if a serum is positive up to 1:50 dilution but negative in a 1:60 dilution, it is said to have a titer of 50. In our patients, the quantitative Kahn test is routinely employed with serial serum dilutions of 1:5, 1:10, 1:20, 1:30 and so on. The titer is recorded in Kahn units, obtained by multiplying the maximal dilution of the serum giving a positive reaction by four. A quantitative titer below 4 units is recorded when the serum shows partial flocculation in the undiluted state and is negative when diluted.[4] Since the sensitivity of the test is known to vary each day,[5] a difference of positivity of one to two dilutions is usually not significant. Thus, change from 40 to 80 Kahn units must be interpreted with caution.

Primary Syphilis

In our clinic, quantitative serologic tests are taken routinely on all patients with early syphilis, but these have proved to be of the greatest value in the cases with negative dark-field lesions. A marked rise in titer provides a simple method of identifying many such lesions as primary syphilis.[6] A simple positive reaction in the presence of a chancrelike lesion in which no spirochetes can be found is construed by most physicians as indicative of primary syphilis. Such a reaction is, however, compatible with the diagnosis of a latent syphilitic infection and a coexisting nonsyphilitic lesion, or it may indicate a biologic false positive reaction caused by chancroidal or lymphogranulomatous infection. The

*From the Clinic for Genitoinfectious Diseases, Grady Hospital, the Department of Medicine, Emory University School of Medicine, and the Georgia Department of Public Health.

†Instructor in medicine, Emory University School of Medicine; director, Clinic for Genitoinfectious Diseases, Grady Hospital.

following case illustrates the value of an increase in titer in the diagnosis of primary syphilis.

Case 1. L. C. H., a 25-year-old Negro, came to the clinic with a penile ulcer of 5 weeks' duration. He denied previous lesions or syphilitic treatment, and the results of previous serologic tests were not available. Physical examination was negative except for the genital lesion, which was a shallow ulceration on the glans penis 1 cm. in diameter, with a clean base and sharp edges. It appeared to be healing spontaneously. Repeated dark-field examinations revealed no spirochetes, and the Frei and Ducrey tests were negative. The quantitative Kahn test, however, showed 120 Kahn units, and within 10 days the titer rose to 600 units. This sharp rise in reagin titer indicated that the syphilitic infection had been very recently acquired.[6] A diagnosis of primary syphilis was therefore made, and treatment was instituted.

Although the ulcer in this case was suspected of being a chancre, this could not be proved until quantitative tests were done. When a chancre is of five weeks' duration or more, as in the above case, *Treponema pallidum* may not be found in more than 50 per cent of the cases,[7] and quantitative serologic tests become of diagnostic importance.

A sharply rising reagin titer is usually found in very recently acquired syphilis, a stationary titer indicates a syphilitic infection of some duration, and a falling titer without treatment usually represents a false positive reaction.[6,8] A considerable proportion of lymphogranulomatous and chancroidal infections have been shown to give false positive reactions for syphilis. Such reactions, which are usually of low titer, may persist for several weeks, and mistaken diagnoses of primary syphilis may easily be made in these cases.[9] We ourselves have on several occasions observed this phenomenon, and have become impressed with the importance of quantitative serologic tests in the presence of genital lesions that are dark-field negative.

Congenital Syphilis

Titered reagin determinations in children born of syphilitic mothers have now become recognized procedures in the diagnosis of congenital syphilis. Since maternal reagin is often transmitted to the child by way of the placenta, serologic tests at birth are of little value. Approximately 15 per cent of positive cord tests revert to negative,[10] and about the same number of negative tests become positive when repeated later in infancy. For this reason, a child born of syphilitic parents should have quantitative tests at regular intervals to determine the disappearance of the maternal reagin or the gradual appearance of his own antibodies. In addition to this method of serial testing for the diagnosis of congenital syphilis, comparative studies of the reagin titer of mother and child may also be of diagnostic value. Almost invariably, the transmitted reagin in the child is equal to or less than that in the mother.[11,12] Hence, a reagin titer in the infant well above that found in the mother should be evidence of syphilis in the child. The following case is illustrative.

Case 2. W. C., a 2-month-old Negro, was seen in the Pediatric Syphilis Clinic in February, 1944, with the complaint of peeling of the skin of the hands and feet. On examination he appeared poorly nourished and fretful. There was a desquamation of the skin of the palms and soles, a pseudoparalysis of the legs and enlargement of the spleen and liver. The mother had had eighteen injections of Mapharsen during the last 2 months of pregnancy and had delivered premature twins, both of whom appeared normal at birth. Cord serologic tests were not done.

On admission the Kahn test of the patient was positive, whereas that of the other twin was negative. During the following week quantitative tests on the family revealed that the patient had 1120 Kahn units and the mother 40 Kahn units, whereas the other twin continued to be negative. Roentgenograms showed extensive destruction and pathologic fractures of the metaphyses of the long bones, with slight periosteal reaction. The long bones of the other twin appeared entirely normal by x-ray.

Following three injections of bismuth, the patient improved remarkably, with a gain in weight and disappearance of the desquamation and pseudoparalysis. Five months later the Kahn test was 360 units in the patient and still negative in the twin.

Because of the rarity of congenital syphilis occurring in only one of twins, the possibility of transmitted reagin from the mother to the apparently infected child had to be excluded in this case. Sufficient evidence for the diagnosis of congenital syphilis was provided by the characteristic roentgenographic findings in the long bones and the reagin titer in the child, which was many times that of the mother. As noted above, however, a quantitative titer in a child less than that of its mother does not exclude the possibility of the child's having congenital syphilis.

Comparative reagin determinations in mother and child may offer an immediate method for the diagnosis of congenital syphilis. Before this method can be depended on, however, further determinations of mother and infant reagin titers are needed to confirm the observation that the transmitted maternal reagin is always less than that of the mother herself.

Relapsing Syphilis

Just as in the initial syphilitic infection, there is frequently a rise of reagin titer in early relapsing syphilis. The clinical recognition of infectious relapse is often difficult, for the recurring syphilide frequently appears as a solitary atypical skin or mucosal lesion rather than the florid eruption of the original infection. In such cases quantitative serologic testing may offer considerable aid in making the correct diagnosis. This is particularly true when patients have never had serologic reversal and have had what could ordinarily be considered adequate syphilitic treatment. The following case is illustrative.

Case 3. M. H. H., a 19-year-old girl, was known to have had syphilis since September, 1942, when she was found to have secondary lesions. Immediately following the diagnosis, she had received treatment without interruption and had taken a total of sixty-six injections of neoarsphenamine, twenty-three of Mapharsen and six of bismuth. Because the serologic tests had never returned to negative, she was referred to the clinic for consultation.

The physical examination was entirely negative, and no evidence of syphilis was found. Blood taken on May 24, 1944, showed 20 Kahn units. The spinal fluid was normal, with no cells, negative Wassermann, Kahn and mastic reactions and 23 mg. of protein per 100 cc. Since the patient had had sufficient arsenical therapy, she was considered to be seroresistant and no further treatment was advised.

One month later the patient returned with erythematous annular lesions of the legs and erosions in the mouth. Spirochetes resembling *T. pallidum* were found in the dark-field preparation of the oral mucosa. The Kahn titer was found to have risen to 120 units, where it remained, and biopsy of the skin lesion was histologically consistent with secondary syphilis. A diagnosis of early infectious relapse was made, and phenarsine hydrochloride was given. With the first injection the mucous patches healed completely and the skin lesions regressed markedly.

In this case the clinical appearance of the skin eruption closely resembled erythema multiforme. The finding of spirochetes resembling *T. pallidum* could not be considered diagnostic, since they were from the mouth and there were no satellite nodes large enough to aspirate. The diagnosis of a mucocutaneous relapse was therefore based on the rise of reagin titer and the histologic appearance of the skin biopsy.

In using quantitative tests as an aid in the diagnosis of relapsing syphilis, it must be remembered that early cutaneous relapse is frequently, but not always, associated with a rise in titer of serum reagin. Some cases of infectious relapse show even a negative serologic reaction.[12] Late gummatous lesions, isolated ocular relapse and neurorelapse may show no changes in serum titer.

One of the frequent problems encountered is that of a patient who has had considerable treatment for syphilis and has finally reversed his serologic reaction, but some time later returns without clinical symptoms but with a positive reaction. The physician usually considers this condition a relapse or reinfection and reinstitutes treatment. In most cases, particularly in late syphilis, a quantitative test reveals an extremely low titer, which remains the same on repeated testing. This small amount of reagin may have been missed because of daily variations in the sensitivity of the tests in the laboratory,[5] thus explaining the previously negative serologic reaction. In these cases what appears to be a serologic relapse is shown by quantitative tests to be seroresistance.[3,12]

Biologic False Positive Reactions

The recognition of biologic false positive reactions is often extremely difficult, but one of the simplest aids in their detection is the use of quantitative serologic tests. A rapidly falling titer in the absence of therapy is evidence of the presence of nonsyphilitic reagin.[8] Even if the serologic reaction does not become completely negative, a decrease of titer or other bizarre behavior should arouse suspicion, and the other recommended procedures[8] for the detection of false positive reactions can then be applied. The following case is of interest in this respect, for the quantitative test was the first clue to the elimination of syphilis in the diagnosis.

Case 4. M. H., a 14-month-old Negress, was admitted to the Pediatric Ward on April 11, 1944, with paralysis of the right eye. She had apparently been well up to 3 days before admission, when the right eye was noticed to be turned in. There were no other symptoms, and the patient otherwise seemed to be in perfect health. She was born of a syphilitic mother who had taken inadequate prenatal antisyphilitic treatment, but the patient was found to have persistently negative Kahn reactions at 5-month intervals.

Physical examination revealed a somewhat irritable but well-nourished child with a temperature of 100°F. The right eye was deviated internally, and no lateral motion beyond the midline could be obtained. The pupillary reflexes were normal, and the other cranial nerves seemed intact. The examination was otherwise negative, and no abnormalities of the chest could be detected, despite roentgenographic findings of a consolidation in the left upper lung. The blood Kahn reaction was doubtful on admission, but became positive several days later and remained so throughout the hospital stay. On April 21 it was 280 Kahn units, on April 27 it was 2 Kahn units, and on May 28 it was 40 Kahn units. The spinal fluid contained 6 white cells per cubic millimeter and 38 mg. of protein per 100 cc. There was a mastic reaction of 444311, a positive Kahn reaction and a negative Wassermann reaction. The spinal-fluid chloride level was 720 mg., and the sugar was 60 mg. per 100 cc. Repeated spinal-fluid examinations showed essentially the same findings, with positive Kahn and negative Wassermann reactions, at both the hospital and the state laboratory. The white-cell count on admission was 17,000, with 82 per cent polymorphonuclear leukocytes. It remained much the same during the first 2 weeks of hospitalization, but fell to 10,000 by the time of discharge. The heterophil antibody test was negative. On May 28, a specimen of serum gave negative Hinton, Mazzini, Kline, Kolmer and Eagle reactions but continued to show a positive standard Kahn reaction. The Kahn verification test showed a nonsyphilitic type of reaction, with more precipitation at cold than at warm temperatures and a higher titer with normal saline solution than with hypertonic salt solution.[13]

Although the tuberculin test was positive, no tubercle bacilli could be found in gastric washings or spinal fluid. The temperature varied between 99 and 100°F. during the hospital stay. The roentgenographic findings did not change, and the consolidation of the lung remained the same. The final clinical impression at the time of discharge was that the patient had a primary tuberculous infection; the etiology of the cranial nerve lesion was still undetermined. Two months later, the blood and spinal-fluid Kahn reactions were negative, but no improvement was noted in either the paralysis of the eye or the pulmonary consolidation.

This occurrence of a false positive Kahn reaction in sick children with the other serologic tests remaining negative is unusual, but has been previously described by Clifton and Heinz.[14]

We have been struck by the high titer occasionally found in false positive reactions in children with febrile illness, the false-positive reactions usually seen in normal adults being quite low.[8] A single titer, therefore, no matter how high, is of no value in excluding a biologic false positive test, and repeated quantitative tests for observation of unusual titer behavior are necessary. For the same reason, a rising titer is occasionally due to an intercurrent illness rather than an actual increase of syphilitic reagin itself.[15] An upward trend should be verified by repeated tests before being accepted as definitive.

Prozone Phenomenon

The prozone phenomenon is one of the yet unexplained reactions that occasionally occur in

serology. It appears in a few strongly positive serums that give negative reactions when whole serum is used but positive reactions when dilutions of the same serum are employed. Zoning is not infrequently noted in the Wassermann test, but is somewhat less frequent in flocculation tests.[3] Such reactions have been noted recently in both the Kline and Hinton tests.[16,17] The following case of zoning in the Kahn test was detected when the titer was measured quantitatively.

Case 5. E. K., a 30-year-old Negress, entered the hospital on January 10, 1944, complaining of postprandial abdominal distress for the previous 3 months. Physical examination revealed no abnormalities except for evidence of weight loss and midepigastric tenderness. The Kahn reaction had been reported doubtful in December, 1943, again doubtful on January 8 and also doubtful on January 10 and 12. The patient gave no history of syphilitic infection, denied previous treatment and showed no signs of syphilis on physical examination.

Because of an unusual deformity of the greater curvature of the stomach, as revealed by fluoroscopic examination, the possibility of gastric syphilis was considered. Despite the doubtful Kahn reports, a quantitative titer was requested on January 14, and the serum was found to contain more than 640 Kahn units. After gastroscopic and further x-ray examinations, the patient was diagnosed as having latent syphilis and simple gastritis, and proper diet and antisyphilitic treatment were instituted. Six months later, the Kahn titer was 20 units and the prozone phenomenon had disappeared.

On the basis of a negative history and four doubtful Kahn reactions, a diagnosis of syphilis could not be made in this case. Quantitative testing, however, revealed a prozone effect that had obscured the presence of a large amount of reagin.

The incidence of serums that show the prozone phenomenon in flocculation tests is quite low, approximately 1 per 1000.[16] For this reason quantitative testing of all doubtful or negative reactions is obviously a waste of time. In the rare case, however, when there is strong clinical evidence of syphilis, quantitative serologic testing is indicated.

Discussion

As shown above, quantitative serologic tests have a distinct place in the diagnosis of primary syphilis and congenital and relapsing infections and in the detection of false positive reactions and prozone effects. In intensive methods of treatment, too, the trend of the reagin titer is important in determining the immediate results of therapy, for rapid-treatment schedules are often completed before the serologic reactions have had time to reverse themselves.

Low titers are oftenest found in late syphilis and high titers oftenest in early cases, but there is so much variation that routine quantitative reactions are of little value in differentiating early from late syphilis.[18] For the usual diagnostic work, therefore, the routinely used qualitative test is all that is needed, since a positive reaction, regardless of the titer, is usually diagnostic of a syphilitic infection. Furthermore, it must be remembered that the titer of reagin is in no way related to the degree of the patient's immunity and has no bearing on the prognosis or outcome of the case.[18] Although one is tempted to attach more significance to a high titer, it cannot be overemphasized that a patient with a titer of 4 Kahn units may be just as heavily infected with syphilis as one with a titer of 1000 Kahn units. This fact must be constantly borne in mind, for the temptation of the physician to interpret too much from the height of the reagin titer is difficult to resist.

Summary

Quantitative serologic tests have been found to be extremely useful in the handling of various problems encountered in syphilitic infections. Serial reagin determinations may be important in the diagnosis of primary syphilis when dark-field examinations of genital lesions are negative.

Congenital syphilis in infants may be determined by comparative reagin titers in the mother and child, as well as by repeated quantitative tests during infancy. Quantitative serologic tests may assist in the recognition of early cutaneous relapse and in the differentiation of seroresistance from serologic relapse. The tests have also been helpful in the detection of prozoning and biologic false positive reactions.

Although quantitative serologic tests are indicated only in selected cases, they are nevertheless an extremely valuable tool in the diagnosis and treatment of syphilis.

References

1. Kahn, R. L. Facts regarding quantitative Kahn reaction. *Ven. Dis. Inform.* **20**:255-257, 1939.
2. Lorenz, W. F. Clinical use of quantitative blood tests for syphilis. *Wisconsin M. J.* **37**:281-286, 1938.
3. Eagle, H. *The Laboratory Diagnosis of Syphilis.* 440 pp. St. Louis: C. V. Mosby Company, 1937.
4. Kahn, R. L. *Technique of the Standard Kahn Test and of Special Kahn Procedures.* Ann Arbor: University of Michigan Press, 1942.
5. Mohr, C. V., and Smith, C. A. On supposed variation of reagin content of syphilitic serum. *Am. J. Syph., Gonor. & Ven. Dis.* **24**:322-329, 1940.
6. Crosby, E. L., and Campbell, A. D. Quantitatively titered serologic test in early syphilis and its response to treatment. *Am. J. Syph., Gonor. & Ven. Dis.* **25**:566-582, 1941.
7. Stokes, J. H. *Modern Clinical Syphilology.* Second edition. 1400 pp. Philadelphia: W. B. Saunders Company, 1934.
8. Moore, J. E., Eagle, H., and Mohr, C. F. Biologic false positive serologic tests for syphilis: suggested method of approach to their clinical study. *J. A. M. A.* **115**:1602-1606, 1940.
9. Knott, L. W., et al. Differential diagnosis of lymphogranuloma venereum and chancroid by laboratory and skin tests. *Am. J. Syph., Gonor. & Ven. Dis.* **27**:657-685, 1943.
10. McKelvey, J. L., and Turner, T. B. Syphilis and pregnancy: analysis of outcome of pregnancy in relation to treatment in 943 cases. *J. A. M. A.* **102**:503-510, 1934.
11. Christie, A. Cited by Eagle.[3]
12. Moore, J. E., et al. *The Modern Treatment of Syphilis.* Second edition. 674 pp. Springfield, Illinois: Charles C Thomas, 1941.
13. Kahn, R. L. Verification test in serology of syphilis. *J. Lab. & Clin. Med.* **28**:1175-1186, 1943.
14. Clifton, W., and Heinz, M. Survey of prenatal syphilis in hospital for sick children. *J. A. M. A.* **114**:1731-1733, 1940.
15. Schoch, A. G., and Alexander, L. J. Unusual behavior of syphilitic reagin following intensive treatment of early syphilis. *Am. J. Syph., Gonor. & Ven. Dis.* **28**:305-309, 1944.
16. Greene, R. A., and Breazeale, E. L. Zone reactions in Kline test. *J. Lab. & Clin. Med.* **25**:104, 1939.
17. Stowe, W. P. Negative "pre-zone" Hinton reactions. *Am. J. Clin. Path.* **10** (Tech. Supp. 4:49-51), 1940.
18. Moore, J. E., and Eagle, H. Quantitative serologic test for syphilis: its variability, usefulness in routine diagnosis and possible significance: study of 1665 cases. *Ann. Int. Med.* **14**:1802-1814, 1941.

CHRONIC MONARTICULAR ARTHRITIS*

JOHN G. KUHNS, M.D.†

BOSTON

CHRONIC monarticular arthritis often presents difficulty in diagnosis. With insidious onset and gradually increasing disability, the history may be confusing and the clinical and laboratory findings indefinite. Roentgenologic and pathological examination in many cases suggests only chronic inflammation, with no clue concerning the original cause. With these patients, after diagnostic aids have been exhausted, one must sometimes wait and observe the further course of the articular inflammation to determine its etiology. Until a diagnosis is made, treatment must be symptomatic and should be directed to the relief of symptoms and the prevention of further disability.

Fortunately, chronic inflammation in only one joint is not frequent, and this type of disease in which a diagnosis cannot be made for a prolonged period is rarer still. I have for the last ten years been recording the cases of chronic monarticular arthritis in which a diagnosis could be made only after prolonged observation. Six months of persistent symptoms was taken arbitrarily as the minimum time for considering the condition chronic. On the wards of the Robert B. Brigham Hospital 15 such patients have been observed among 2268 patients suffering from chronic arthritis. One of these, a girl of eleven with a chronic arthritis of the left hip of eight months' duration, has recently been admitted and has been under observation for only a short time. No diagnosis has yet been made, and this case is not included in the tables or in the further discussion.

Acute monarticular arthritis is relatively frequent. In most cases the cause of the inflammation in the joint is evident, and is usually a preceding injury or an acute infection. When the cause is not apparent, laboratory aids frequently give the diagnosis. Rapid recovery is the rule, and when healing is delayed, the subsequent course of the disease usually leaves no doubt concerning the diagnosis. Evidences of previous inflammation in the joints are sometimes found when there are no complaints and no evidence of disability.

The location of the disease, the duration of symptoms, the clinical impression, the course and the final diagnoses in the 14 cases of chronic monarticular arthritis are given in Table 1. Early impressions given in our own and many neighboring clinics were often subsequently found to be wrong. The two diseases that offered the greatest difficulty in differentiation were rheumatoid arthritis and articular tuberculosis. In the average case of rheumatoid arthritis there is a gradual onset, with progression of the inflammatory process from joint to joint, followed by gradual subsidence of the inflammation, leaving varying amounts of deformity in the involved joints. When there is great variation from this clinical course, difficulties arise in making a diagnosis. In tuberculosis there is usually a mild inflammation in one joint, slowly increasing in severity concomitant with a decline in the general health. In both diseases there is often a secondary anemia, an elevated sedimentation rate and evidence in x-ray films of swelling of the soft tissues, followed by osseous atrophy. Aspiration and study of articular fluid and even biopsy may yield inconclusive results until the disease is well advanced. There is no characteristic microscopic appearance in rheumatoid arthritis. If tubercles are found, one can be relatively certain of the presence of tuberculosis. Bacteria recovered from synovial fluid are

TABLE 1. *Summary of Data in Cases of Chronic Monarticular Arthritis.*

Case No.	Age	Sex	Joint Involved	Duration of Symptoms	Presumptive Diagnosis	Course	Time Followed	Final Diagnosis
	yr.						yr.	
1	6	M	Right knee	12 mo.	Rheumatoid arthritis	Increasing disability	5	Tuberculosis
2	9	F	Left hip	18 mo.	Tuberculosis	Recovery	5	Chronic sprain
3	11	M	Right knee	6 mo.	Tuberculosis	Other joints involved	4	Rheumatoid arthritis
4	14	M	Left knee	6 yr.	Tuberculosis	Increasing disability	3	Tuberculosis
5	16	F	Left knee	8 yr.	Tuberculosis	Other joints involved	4	Rheumatoid arthritis
6	18	F	Left hip	6 mo.	Acute infection	Eventual ankylosis	3	Acute infectious arthritis
7	19	F	Left ankle	18 mo.	Tuberculosis	Increasing disability	2	Tuberculosis
8	22	F	Right shoulder	6 mo.	Rheumatoid arthritis	Rapid recovery	6	Hysteria
9	31	F	Right knee	6 mo.	Acute infection	Improvement	3	Gonococcal arthritis
10	34	F	Left knee	10 mo.	Acute infection	Ankylosis	4	Acute infectious arthritis
11	37	M	Left knee	7 mo.	Tuberculosis	Recovery	7	Rheumatoid arthritis
12	42	M	Left hip	8 mo.	Tuberculosis	Died	1	Sarcoma
13	46	F	Right elbow	15 mo.	Rheumatoid arthritis	Slow progression	2	Tuberculosis
14	61	F	Right knee	6 mo.	Osteoarthritis	Slow progression	2	Tuberculosis

*From the Robert Breck Brigham Hospital.

†Chief of the Surgical and Orthopedic staffs, Robert Breck Brigham Hospital.

also conclusively pathognomonic. Failing these, if the course of the disease follows no definite pattern, one is often uncertain of the diagnosis.

In a number of these patients punch biopsies were performed to make a diagnosis or to estimate the progression of the process in the joint. This procedure was done with a No. 12-gauge tri-flanged needle with a stylet, which was removed when the desired depth in the tissues was reached. A small core of tissue was then obtained by twisting the needle and applying suction through an attached syringe. The small masses of tissue removed in this manner showed either normal tissue or chronic inflammation. The tissues were identified with

Table 2. *Summary of Diagnostic Aids in Cases of Chronic Monarticular Arthritis.*

Case No.	History	Physical Examination	X-ray Examination	Blood	Other Tests	Aspiration	Biopsy
1	Slow onset	Swollen and warm joint	Bony atrophy	Moderate leukocytosis	Tuberculin positive	Fluid negative for tuberculosis	No record
2	Patient struck by wagon	Pain and muscular spasm	Haziness of joint	Normal	All negative	No record	No record
3	Slow onset; father had tuberculosis.	Slight swelling of joint	Bony atrophy	Normal	Sedimentation rate 52 mm.	Fluid negative for tuberculosis	No record
4	Patient struck while playing	Moderate swelling of joint	Haziness of joint	Moderate leukocytosis	Tuberculin plus; sedimentation rate 65 mm.	Fluid positive for tuberculosis	No record
5	Patient fell off sled	Pain and limitation of motion	Slight bony atrophy	Mild anemia	Sedimentation rate 48 mm.	No fluid	No record
6	Followed tonsillitis	Stiff joint	Beginning ankylosis	Normal	All negative	No record	No record
7	Sprained ankle	Swollen and painful joint	Bony necrosis (sequestrums)	Normal	Tuberculin plus	No record	No record
8	Gradual onset	Slight limitation and pain on motion	Negative	Moderate leukocytosis	All negative	No record	No record
9	Sudden onset; fever.	Flexion deformity and painful tender joint	Destruction of cartilage	Slight leukocytosis	Gonococcal fixation plus; sedimentation rate 89 mm.	No fluid	No record
10	Fever	Stiff joint	Ankylosis of joint	Normal	All negative	No record	Chronic inflammation
11	Gradual onset	Flexion deformity and moderate swelling of joint	Periarticular swelling	Normal	Sedimentation rate 57 mm.	No fluid	No record
12	Slow onset	Flexion deformity and muscular spasm of joint	Bony atrophy	Mild anemia	Tuberculin plus; sedimentation rate 30 mm.	No fluid	Sarcoma
13	Gradual onset	Swelling and stiffness of joint	Bony atrophy	Mild anemia	Tuberculin plus	Fluid positive for tuberculosis	No record
14	Slow onset	Flexion deformity and swollen joint	Bony necrosis	Normal	Tuberculin plus; sedimentation rate 94 mm.	Fluid positive for tuberculosis	No record

difficulty, and rarely could an opinion be given of the nature and severity of the inflammation in the joints. These attempts were soon discontinued. They demonstrated that satisfactory biopsies could be obtained only by adequate inspection of the articular cavity.

In this series, the duration of symptoms ranged from six months to eight years. The ages varied greatly, but the majority of the patients were children or young adults. The lower extremity was involved in most cases, a distribution that is observed in most injuries and infections involving the limbs. The knee joint was affected in 8 cases, the hip in 3, and the ankle, shoulder and elbow in 1 each. Of these 14 cases, only 2 proved to be rheumatoid arthritis, 1 was probably rheumatoid arthritis, 5 eventually were found to be tuberculosis, 2 were acute infectious arthritis, 1 was a gonococcal infection, 1 was a slowly growing sarcoma, 1 was diagnosed hysteria, and 1 was a chronic sprain.

The diagnostic procedures employed in attempting to arrive at a diagnosis are given in Table 2. All these patients were questioned and examined both by the house officers and by the visiting staff. There was a history of slow evolution of symptoms in half of them. In the others, there was a definite preceding injury in 4 and a sudden onset with fever suggesting an acute infection in 3. In the majority of cases examination of the joint showed only mild articular inflammation, with nothing to suggest the nature or the severity of the arthritis. The x-ray examinations were not characteristic, showing in most cases only the changes that accompany decreased function of a limb. The blood picture was usually normal. In 8 cases, the sedimentation rate (Westergren) was moderately elevated; in 3 it was normal, and in 3 it was not done since these patients were seen before the sedimentation test came into general use. The tuberculin test was positive in 6 cases. In 5 of these, the arthritis was found to be caused by tuberculosis. A strongly positive tuberculin test, although in no sense diagnostic, suggests that the inflammation is a tuberculous infection. The Wassermann reaction was negative in all these patients. The gonococcal fixation test was carried out in 6 cases; it was negative in 5 and positive in 1. It is generally reported to be positive in at least 80 per cent of cases when gonorrheal arthritis is present. Aspirations of joints gave indefinite results in 6 cases, and in 3 it showed tuberculous in-

fection. There is no record of aspiration in the other cases. Surgical biopsy was performed only when the severity of the disability suggested that this procedure might greatly modify the treatment.

Case Reports

Case 1. A 6-year-old boy 1 year before admission fell upon his right knee which gradually became more swollen and limited in motion. It was treated in an outpatient clinic with support, a sprain being the presumptive diagnosis.

Examination at admission showed a swollen, hot knee, mildly tender on pressure. There was a 30° flexion deformity. There was a slight afternoon temperature. X-ray examination of the chest was negative. The blood showed a slight anemia, with a white-cell count of 14,600. A Wassermann test was negative and a tuberculin test positive. Aspiration of the knee showed clear fluid with a few polymorphonuclear cells. Injection of the joint fluid into a guinea pig failed to give evidence of tuberculosis. X-ray examination of the knee showed swelling of the soft tissues and slight osseous atrophy. The symptoms subsided somewhat and the patient was permitted to walk with a knee support. He was discharged to a state hospital.

Four years later he was walking without a limp, there were no complaints, and the right leg was 2.5 cm. longer than the left. The unproved diagnosis at the state hospital was healed tuberculosis.

Case 2. A 9-year-old schoolgirl was struck by a wagon on the left leg 1½ years before admission, the injury being followed by pain and limitation of motion in the left hip. The mother had died of tuberculosis but had had no contact with the patient after she was two weeks old.

Examination showed moderate limitation of flexion and abduction of the left hip. X-ray examination showed haziness of the hip joints, the chest being negative. The blood showed nothing abnormal. Tuberculin and Wassermann tests were negative. Under bed rest the symptoms subsided entirely in 3 months.

The patient has remained well for 5 years since discharge. The probable diagnosis was chronic sprain of the left hip.

Case 3. An 11-year-old schoolboy complained of pain and swelling of the right knee of 6 months' duration. There was no history of injury. His father had a healed tuberculous lesion of the right ankle.

Examination showed moderate swelling and fluid in the right knee. There was a 20° flexion deformity. On x-ray examination there was swelling of the soft tissues. X-ray films of the chest were negative. The blood showed nothing abnormal. Wassermann and tuberculin tests were negative. The sedimentation rate was 52 mm. Injection of aspirated joint fluid into a guinea pig failed to give evidence of tuberculosis. The patient was given bed rest and a plaster cast for the right leg. The symptoms entirely subsided in 4 months. A tonsillectomy was then performed and he was discharged home.

He remained well for 4 years, when he began to have pain and stiffness in the right hip and low in the back. He was readmitted to the hospital. X-ray examination showed advanced arthritis of the spine, and the disease progressed to ankylosis of the entire spine and both hips. A severe glomerular nephritis developed. The patient is now completely helpless in a rest home. The final diagnosis was rheumatoid arthritis.

Case 4. A 14-year-old boy was struck in play on the right knee 5 years before admission, and was treated at intervals in a hospital clinic. The symptoms partially subsided and he continued going to school, but the knee remained swollen and limited in motion. Four months before admission the symptoms became worse.

Examination showed marked swelling and limitation of motion. The white-cell count was 13,600, with 44 per cent lymphocytes. The sedimentation rate was 65 mm. Gonococcal-fixation and Wassermann reactions were negative. A tuberculin test was positive. X-ray examination of the knee showed narrowing of the joint space and thickening of the soft tissues. The chest showed thickening about the roots of the lungs but no definite evidence of tuberculosis. Injection of fluid aspirated from the knee produced tuberculosis in a guinea pig. The boy was transferred to a sanatorium for the treatment of tuberculosis.

The diagnosis was tuberculosis of the knee.

Case 5. A 16-year-old schoolgirl entered the hospital complaining of pain and swelling of the left knee of 8 years' duration, coming on after a fall from a sled. There was intermittent swelling but no pain. Tuberculosis was suspected in another clinic, although x-ray examination showed only slight bony atrophy. Aspiration of the joint was negative. Symptoms subsided completely after 18 months in a convalescent home. The patient remained well for 6 years but 4 months preceding admission she began to have swelling, pain and limitation of motion in the left knee, right ankle and right wrist.

On admission there was no increased heat or tenderness in the joints or other noteworthy findings. Examination of the blood showed a slight anemia, with a white-cell count of 7800. Wassermann and tuberculin tests were negative. The sedimentation rate was 48 mm. X-ray examination showed slight bony atrophy and periarticular swelling about the involved joints. During the stay in the hospital the hands and elbows and hips also became inflamed. The patient gradually improved and was discharged after 8 months.

She has since been followed in the outpatient clinic for 5 years. The only remaining disability is slight limitation of motion in the left hip and right elbow. The diagnosis was rheumatoid arthritis.

Case 6. An 18-year-old girl entered the hospital complaining of pain and increasing stiffness of the left hip of 6 months' duration. The onset of symptoms followed an attack of tonsillitis. She was treated in a suburban hospital, where the throat infection subsided and the symptoms in the hip decreased.

Examination on admission showed moderate atrophy of the musculature of the left hip joint but was otherwise negative. The blood showed no abnormal findings. Wassermann and tuberculin tests were negative. A vaginal smear showed no gonococci. X-ray examination showed almost complete loss of cartilage at the left hip joint, with bony atrophy; there was no definite osseous destruction. The leg was made comfortable in a plaster cast with the hip held in slight flexion and abduction. All motion at the hip was soon lost, and x-ray films showed beginning bony ankylosis.

The patient was subsequently followed for 3 years. She remained well during this period, but the left leg was ankylosed. The diagnosis was acute infectious arthritis followed by ankylosis.

Case 7. A 19-year-old Italian candy maker was admitted complaining of pain and swelling of the left ankle coming on after a sprain of the ankle 2 years before. There was a definite limp, but pain was not severe.

Examination showed extensive swelling on both sides of the ankle, with fluctuation on the outer side. The temperature was normal. Examination of the blood showed no definite abnormality. A Wassermann test was negative, and a tuberculin test was positive. The x-ray films showed necrosis of the os calcis, with several small sequestrums. Biopsy demonstrated tuberculosis.

The patient gradually improved in a convalescent hospital. There she developed a psychosis and has since been confined in a state mental hospital. The final diagnosis was tuberculosis of the ankle.

Case 8. A 22-year-old waitress complained of pain and stiffness of the right shoulder of 6 months' duration, which appeared after a severe throat infection. The condition had remained practically unchanged until admission.

Examination showed moderate limitation of motion and slight pain on motion of the right shoulder. The white-cell count was 15,000. The sedimentation rate was 17 mm. Wassermann and gonococcal-fixation tests were negative. X-ray examination of the shoulder showed no abnormality. A psychiatric examination revealed an unstable personality

with difficulty in adjustment and frequent changes of jobs. A 3-month pregnancy had been terminated by abortion shortly before the onset of symptoms. The symptoms quickly subsided in the hospital. A better environment and more congenial employment was provided by the Social Service Department.

The patient has been followed for 6 years and has had no further trouble in the shoulder. The final diagnosis was hysteria.

Case 9. A 31-year-old schoolteacher had pain and swelling of the right knee of 6 months' duration. There was no history of injury. A cast was applied to the knee for the relief of pain at a suburban hospital, but was soon removed. The condition remained practically unchanged.

On examination there was a 30° flexion deformity of the knee, which was tender and showed increased heat. The white-cell count was 11,350. The sedimentation rate was 89 mm. The gonococcal-fixation test was positive. Wassermann and tuberculin tests were negative. X-ray examination showed periarticular swelling with beginning destruction of the articular surfaces. A cervical smear showed no gonococci. No fluid was obtained on aspiration. Under rest and physiotherapy the symptoms slowly subsided.

After 4 months there was improved motion in the knee, which has remained unchanged for 8 years. The final diagnosis was probably healed gonococcal arthritis.

Case 10. A 34-year-old housemaid had pain and tenderness, followed by inability to move the left knee, of 10 months' duration. She had had a fever for the first 2 weeks of her illness.

Examination showed slight swelling and tenderness over the left knee. There was no motion in the joint. Wassermann and tuberculin tests were negative. The blood examination showed no abnormal findings. X-ray films showed destruction of the articular surface and beginning ankylosis. There was no evidence of gonococcal infection. The symptoms subsided entirely as ankylosis occurred.

The patient has remained symptomless for 6 years. An operation performed later to secure motion showed chronic inflammation in the joint. The diagnosis was acute infectious arthritis with ankylosis.

Case 11. A 37-year-old farmer entered the hospital for the relief of pain and limitation of motion in the left knee of 7 months' duration. The onset was gradual, and there was a history of a sprain of the left thigh in lifting a heavy object shortly before.

Examination showed moderate swelling of the knee with slight flexion deformity but no tenderness or increased heat. The physical examination was otherwise negative. The blood was normal. Wassermann, gonococcal-fixation and tuberculin tests were negative. The sedimentation rate was 57 mm. A prostatic smear was negative. Aspiration of the joint showed nothing abnormal. X-ray films of the chest were negative. X-ray examination of the knee showed swelling of the periarticular tissues only. With bed rest and physiotherapy there was a rapid regression of symptoms in 3 months. Chronically infected tonsils were then removed without incident.

The patient has remained completely well for 9 years since discharge. It was the impression of the staff that this was a healed rheumatoid arthritis of the knee associated with a chronic upper respiratory infection, although the possibility of a chronic sprain of the knee could not be excluded.

Case 12. A 42-year-old storekeeper was admitted complaining of pain and stiffness in the left hip of 8 months' duration. He had lost 10 pounds in weight during the previous 2 months.

Examination showed muscular atrophy, muscular spasm and a 20° flexion deformity at the right hip. There were no other significant findings. Examination of the blood showed a mild hypochromic anemia. The sedimentation rate was 30 mm., and gonococcal-fixation tests were negative. A tuberculin test was positive. X-ray films of the chest showed nothing remarkable. The hip showed a small area of decalcification in the body of the ischium, with increased density in the acetabulum. According to the roentgenologist, this was suggestive of tuberculosis. Aspiration of the joint gave no fluid. The serum calcium, phosphorus and phosphatase levels were within normal limits. The patient had increasing pain, which was not relieved by traction or a plaster spica.

He was transferred to a tuberculosis sanatorium in his home state, where continuance of severe pain eventually led to an operation on the hip. Examination of tissue from the ischium showed a chondrosarcoma. The patient died 2 months later. The diagnosis was sarcoma of the left ischium.

Case 13. A 46-year-old housewife had increasing soreness and limitation of motion in the right elbow of 5 years' duration. There was no related history of injury or infection. Her general health had remained good. X-ray examination by the family physician 1 year previous to admission showed bony atrophy about the elbow. A diagnosis of rheumatoid arthritis was made and physiotherapy was given, without relief.

Examination showed a 90° flexion deformity at the right elbow and 5° of painful motion. The elbow was swollen to about twice the normal size and was slightly tender, but showed no increased heat. General examination showed no other significant findings. X-ray examination of the chest was negative. The elbow showed bony atrophy and narrowing of the joint space. The sedimentation rate was 18 mm. Wassermann and gonococcal-fixation tests were negative. The tuberculin test was positive. Fluid aspirated from the joint and injected into a guinea pig showed tuberculosis.

There has been a gradual improvement in the elbow following immobilization and heliotherapy. The diagnosis was tuberculosis of the elbow.

Case 14. A 61-year-old housewife entered the hospital complaining of pain and stiffness in the right knee of 6 years' duration.

Examination showed moderate swelling and limitation of complete extension in the right knee. It was not tender, and there was no increased heat. The fingers showed Heberden's nodes. X-ray examination of the chest revealed an old tuberculous lesion in the right upper lobe. That of the knee showed narrowing of the joint space, an area of destruction over the femoral condyle and extensive osteoarthritis. The blood was normal. The Wassermann reaction was negative. The sedimentation rate was 94 mm. The tuberculin reaction was positive. The symptoms subsided with physiotherapy and a support for the knee.

The patient remained well for 3 years, when she returned presenting a draining sinus over the knee. Fluid aspirated from the joint and injected into a guinea pig resulted in tuberculous infection. The patient has been at a state tuberculosis sanatorium for the last 2 years. The diagnosis was tuberculosis of the knee.

The experience encountered in these cases has made us more cautious in accepting an immediate diagnosis in any patient with chronic monarticular arthritis. There are no signs or clinical findings that are in themselves pathognomonic of rheumatoid arthritis. If healing occurs gradually, even long observation may not solve the question; likewise, it is difficult to demonstrate a histologic picture in articular tissue that is sufficiently characteristic to establish the diagnosis. In the presence of unrelated infection, chronic trauma — for example, sprain — that has not healed because of inadequate treatment may easily simulate rheumatoid arthritis. Rheumatoid arthritis, as these patients show, rarely remains monarticular, but tends to revert to the usual picture after a few years. Undoubtedly, if the patient remains well, monarticular rheumatoid arthritis may heal and not recur, but this is a rare occurrence. Whether in certain of the patients tuberculosis was superimposed on an already existing rheumatoid or osteoarthritis or whether a quiescent infection was activated by injury or irritation, cannot be decided at the present time. Slow-

growing tumors adjacent to joints may counterfeit chronic arthritis until the further development of the tumor establishes the diagnosis. Hysteria simulating joint symptoms is rare.

In atypical chronic arthritis, particularly when it is monarticular, the diagnosis must be made with caution; in rare cases it cannot be made definitely, long observation helping only to confirm the presumptive diagnosis. Symptomatic treatment is indicated until the diagnosis is established, when other measures directed against the cause of the inflammation can be added. Deformity is prevented by traction, a plaster cast or other appropriate apparatus. When a definite diagnosis has not been made, attempts should be made to promote strength and motion in the joint as the symptoms subside. A number of other therapeutic procedures are useless or positively harmful in certain diseases, and these should be avoided until a definite diagnosis has been established.

Conclusions

Chronic monarticular arthritis in which a diagnosis cannot be easily made is infrequent. Often the cause of the inflammation can only be determined by observing the further course of the disease. During this time, treatment must be symptomatic and must be directed to preserving articular function so far as possible. Any procedure that may be harmful should be avoided. No definitive treatment — for example, surgery — should be carried out until the diagnosis has been established. Chronic monarticular arthritis is rarely due to rheumatoid arthritis.

372 Marlborough Street

THE EFFECT OF PENICILLIN ON INOCULATION MALARIA*

A Negative Report

J. A. HINDLE, M.D.,† A. S. ROSE, M.D.,† L. D. TREVETT, M.D.,† AND C. PROUT, M.D.†

BOSTON

UNDER a well-organized national program, clinical and laboratory data showing the therapeutic effectiveness of penicillin in many disease conditions are rapidly accumulating. Recently penicillin has been made available for more widespread civilian use in certain specified infections. There are few factual data available concerning its efficacy in malaria.

Relapsing tertian malaria in many of the returning troops is proving a definite problem. The chief concern is about the best method for the active treatment of these relapses and about the possibility that such malarial infestations will form a reservoir for a marked increase in cases among the general population. It is natural, therefore, for questions concerning the effect of penicillin on malaria to arise. It is hoped that this negative report will serve to answer some of these questions.

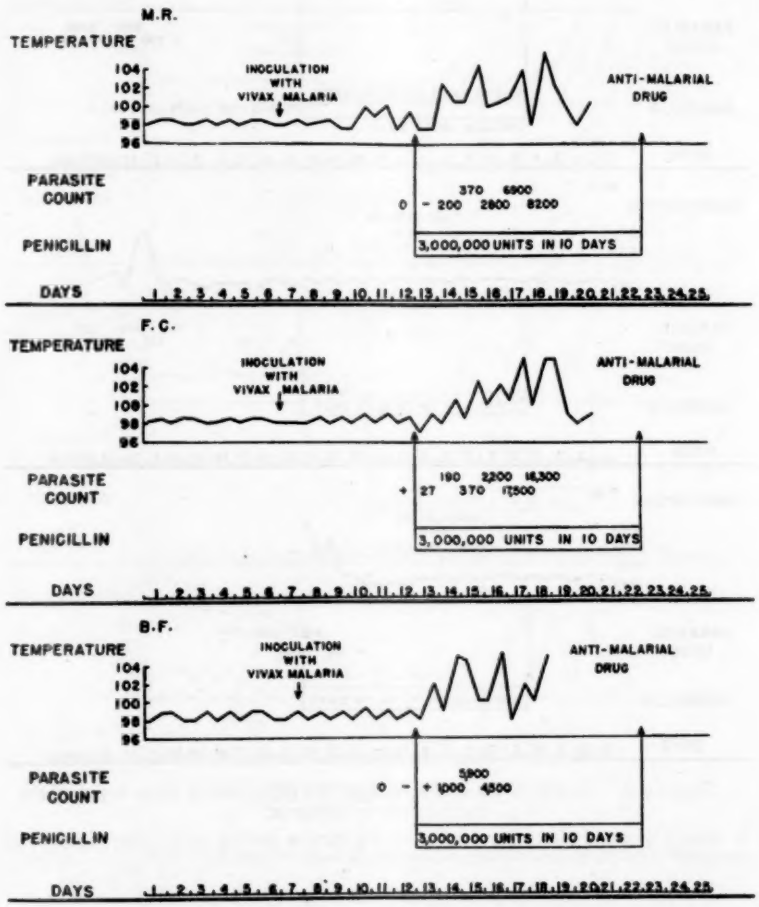


FIGURE 1. *Charts of Case Receiving Penicillin after the Development of Parasitemia and Fever.*

It should be observed that parasites increase and fever occurred in the usual sequence. The malarial course was then altered by the administration of an antimalarial drug under investigation.

As a research grant from the Office of Scientific Research and Development for the treatment of neurosyphilis, penicillin was issued to the Boston

*From the Boston Psychopathic Hospital.

The work described in this paper was performed with penicillin supplied by the Office of Scientific Research and Development. It was done under contract, recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and the Massachusetts General Hospital.

†Clinical investigator in the study of penicillin in neurosyphilis and of antimalarial drugs at the Boston Psychopathic Hospital.

Psychopathic Hospital in February, 1944. Simultaneously, a unit for the study of antimalarial drugs was established at this hospital under O.S.R.D. Contract No. OEMcmr-419. Under this double investigative program 28 patients with neurosyphilis have been treated by the combined use of penicillin and benign tertian malaria. In 15 of these cases the two forms of therapy overlapped in such a way as to make it possible to draw conclusions concerning the effect of penicillin on this form of malaria. The clinical charts of some of these cases form the basis of this report.

Method and Material

Penicillin was administered in all cases intramuscularly, 50,000 Oxford units being given every four hours for ten days, a total of 3,000,000 units. Therapeutic malaria was induced by *Plasmodium vivax* (McCoy strain) in all cases. A calculated standard inoculum of 500,000 parasites, taken from an active case, was injected intravenously. The cases were selected, so far as possible, to avoid natural immunity. After inoculation, each patient's temperature was taken rectally every four hours. At the beginning of fever (101.6°F., rectal), the temperature was taken every hour. Parasite counts, by a slight modification of Earle's method, were performed daily.

Results

The 15 cases in which penicillin and fever therapy were given together are divided into two groups.

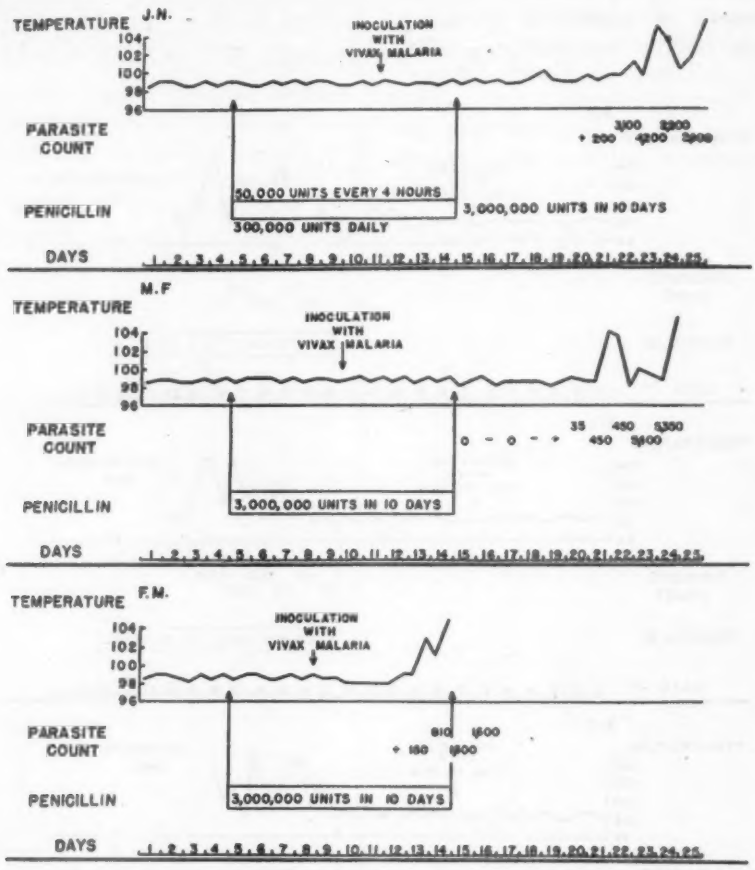


Figure 2. *Charts of Cases Receiving Penicillin Several Days before the Inoculation of Malaria.*

It should be noted that, after a variable incubation period, increasing numbers of parasites and paroxysms of fever appeared.

In Group 1 (6 cases), penicillin was administered after the development of fever and parasitemia. Figure 1 shows the clinical charts of 3 patients. Penicillin caused no reduction in fever, no significant alteration in the timing of the paroxysms and no reduction in the level of parasite counts in any of the cases. These results demonstrate that penicillin does not suppress the clinical manifestations of inoculation *P. vivax* malaria.

In Group 2 (9 cases), penicillin was started before the development of fever. These cases are subdivided into 4 cases in which penicillin was started a few days before the malarial inoculation (Fig. 2) and 5 cases in which it was started at approximately the time of the malarial inoculation (Fig. 3). The clinical charts of these cases demonstrate that

penicillin does not prevent or postpone the development of inoculation *P. vivax* malaria. This seems of special significance, since the number of parasites in the recipient is lowest at the time of inoculation, and if penicillin has any antimalarial action at all, it should have been shown by this experiment.

Discussion

Inoculation malaria differs in certain respects from natural-occurring, mosquito-induced malaria. It is produced by the transfer of trophozoites from patient to patient. The incubation period is usually shorter by a few days or a week; parasite counts as a rule do not reach quite such high levels; and, although the temperature response may be just as severe as in mosquito-induced malaria, the disease is more satisfactorily suppressed by antimalarial drugs. Cases of inoculation malaria (induced for therapeutic fever) comprise ideal subjects for the testing of drugs with antimalarial activity, for over a period of many years the disease has been well standardized and it has been clearly shown that drugs that do not suppress trophozoite-induced malaria do not suppress sporozoite-induced malaria.

In this study only the McCoy strain of *P. vivax* was used. Accordingly, it is not possible to draw definite conclusions concerning penicillin in *P. malariae* and *P. falciparum* infections. If one reasons by analogy to known antimalarial drugs, however, it can be presumed that since penicillin shows no antimalarial activity against *P. vivax* infections, it will have none against the other types.

In a review of penicillin therapy in the United States Army published in December, 1943, Lyons* states: "Malaria due to *Plasmodium vivax* is not affected by penicillin. In addition to the 4 recorded failures, 2 other patients have developed recurrent malaria under treatment." No other reference to the effect of penicillin on malaria has been found in the literature.

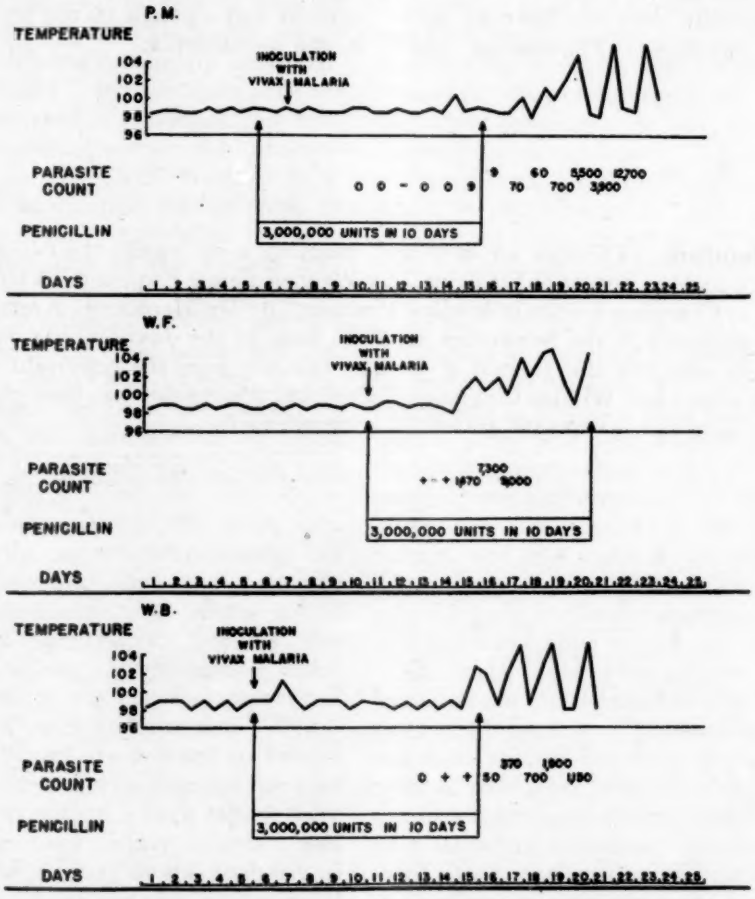


Figure 3. *Charts of Cases Receiving Penicillin on or about the Same Day as the Malarial Inoculation.*

It should be observed that, after a variable incubation period, parasites appeared and increased in number, and paroxysms of fever occurred in the characteristic manner.

Summary and Conclusions

During investigations on the use of penicillin in neurosyphilis, 28 patients received both penicillin

*Lyons, C. Penicillin therapy of surgical infections in U. S. Army. *J. A. M. A.* 123:1007-1018, 1943.

and benign tertian malaria. Fifteen of these had penicillin administered simultaneously with the malaria. Clinical charts of 9 cases are presented. These charts graphically demonstrate that penicillin does not suppress fever or the parasite count of active inoculation malaria and that when given before or at the time of the malaria inoculation it does not prevent or postpone the development of fever and parasitemia.

It is reasoned by analogy to known antimalarial drugs that since penicillin does not have an antimalarial effect on inoculation *Plasmodium vivax* malaria, it will not be effective in other types of malaria or in naturally acquired malaria.

Since the writing of this paper we have had further experience in the use of penicillin in therapeutic malaria. In view of the fact that penicillin is rapidly removed from the body, we have tried more frequent injections to exclude this possible loophole in the ineffectiveness of the drug. We have given 3,000,000 units in five days at the rate of 50,000 units at each intramuscular injection every two hours, day and night. This method has been used in about 20 cases without any change in the paroxysms of fever or in the parasitemia.

Addendum. Through an oversight, permission to reprint the two articles "Justice and the Future of Medicine," by Wendell Berge, Esq., and "A Urologist Looks at Changing Trends in Medical Practice," by Dr. Herman L. Kretschmer, which appeared in the November 30, 1944, issue of the *Journal*, was obtained from the editor of the *Journal of Urology* but not from the copyright owner, The Williams and Wilkins Company, Baltimore. Permission has been obtained *ex post facto* and is herewith gratefully acknowledged.

MEDICAL PROGRESS

ORTHOPEDIC SURGERY: THE PROBLEM OF THE INTERVERTEBRAL DISK

CARROLL B. LARSON, M.D.*

BOSTON

THE cause of the backache has for years intrigued orthopedic surgeons. Many popularized diagnoses, such as sacroiliac slip, lumbosacral strain and so forth, represent phases of progress in unraveling the mysteries of back pain. Backache associated with pain in the leg has frequently been inaccurately labeled "sciatica" by doctors and the laity alike. The recent trend is to abolish this term because it carries no accurate connotation concerning either the cause or the distribution of pain. In 1934 a new spark of interest was aroused by Mixter and Barr[1] when they introduced the syndrome ascribed to herniation of the nucleus pulposus. A profusion of literature attests to the popularity of this new syndrome, variously referred to as ruptured intervertebral disk, protruded disk and herniation of the disk. The purpose of this report is to give a concise notion of the factual information, as well as the controversial opinions, that exists regarding the intervertebral-disk syndrome as it is known today.

The embryologic development of the spine, with special reference to the intervertebral disk, has been studied by Ehrenhaft,[2] and the point he emphasizes is the avascularity that occurs in the disk after the age of twenty-five. Possibly this has a bearing on the etiology of pathologic disks. The question of trauma as the cause of rupture of the intervertebral disk remains unsettled. Hyndman, Steindler and Wolkin[3] are inclined to believe that even in the few patients who describe the root pain as being coincident with the back injury there has been a preceding back injury. Inman and Saunders,[4] in a detailed account of the anatomy of the intervertebral disk, point out the frequency of protruded disks in the region on the intervertebral foramen, where the postligamentous support between vertebral bodies is weakest. They estimate, by an analysis of force vectors resultant upon the lower lumbar disks in lifting a weight of 50 pounds, that, under average conditions, a pressure amounting to about 500 pounds is exerted. In addition, when the spine is flexed, the nucleus pulposus in the lumbar region migrates dorsally, tension is thrown on the posterior portion of the annulus, and if some rotation accompanies flexion, the annulus is further subjected to torsional stresses. These forces alone can cause herniation. If a single injury results in herniation, it presupposes a considerable tear in the tough annulus fibrosus. At operation the posterior ligament frequently is found intact, but when incised reveals a loosened free portion of dense fibrous tissue that must be as much a part of the annulus as of the nucleus pulposus. These cases make one wonder whether some type of pre-existing degeneration is responsible for the separation of a fragment. At present there are many unanswered questions pertaining to the pathogenesis of the protruded-disk syndrome.

Young and Brailsford[5] carefully followed 497 patients with backache and give a numerical notion concerning the relative frequency of ruptured disks. These figures were taken from a clinic in which both soldiers and industrial workers were cared for. Of the total number, pain was localized in the back in 206 cases, was associated with referred leg pain in 204 cases and was associated with referred trunk pain in 87 cases. One hundred and three soldiers with leg pain were studied for the presence of a ruptured intervertebral disk. Of these cases, laminectomy was performed in 15; 9 cases showed definite protrusion, 2 cases had a thickened ligamentum flavum, and in 4 cases no abnormality was found. These figures tend to indicate that in all cases with referred pain in the leg approximately 10 per cent will prove to be due to ruptured disks.

The exact cause of the pain in the disk syndrome has not been clearly established. The evidence suggests direct nerve-root pressure as a major source of radiation pain in the many patients who have had relief of pain after removal of the mass. In view of the fact that many patients are not relieved of this pain following operation, one must always keep in mind other mechanisms of pain production. Such mechanisms must explain the leg pains in cases in which exploration has failed to reveal a protruded disk, as well as similar leg pains in a large group of other conditions, such as ligamentous injuries, fractured facets, hypertrophic overgrowths, impinging spinous tips, unstable lumbosacral junctions associated with various congenital anomalies, arachnoiditis, malignant neoplasm, infectious lesions, rheumatoid arthritis and sacroiliac strain.

Steindler et al.[3] have shown that referred pain can be completely eliminated by interrupting a reflex arc. He has traced the reflex pathways that connect the lesion to the so-called "trigger points of localized sensitivity," as well as to the referred pain in the leg. These pathways can be interrupted by an injection of novocain into the trigger point or points. From a practical standpoint he has been able to relieve pain in about one fifth of the cases

*Instructor in orthopedic surgery, Harvard Medical School; assistant in orthopedic surgery, Massachusetts General Hospital.

of referred pain in which the cause was other than a protruded disk.

Intervertebral disks have been shown to contain nerve fibers.[2] This makes it possible for the pain to arise within the disk space, particularly when the disk is subjected to excessive pressure or when it is the seat of degenerative disease. Inman and Saunders[4] were struck by the clinical findings in cases of protruded disks, inasmuch as the areas complained of by the patients were quite similar, whether the protrusion was causing pressure on the fourth or fifth lumbar or first sacral nerve root. This led them to adopt a new sclerotome, rather than dermatome, distribution of referred-pain areas. The reader is urged to read the original article in order to comprehend completely this feasible conception.

The idea has many times been expressed that any backache associated with radiation pain into the thigh or leg is due to a ruptured disk. Certainly one should look carefully into the history for more distinguishing features of a ruptured intervertebral disk. Many cases with a presumably classic history of a protruded nucleus have, on exploration, revealed no findings to substantiate the diagnosis. On the other hand, explorations have revealed ruptured disks to account for local pain in the back, as well as motor and sensory disturbances, without pain in the thigh or leg. The above facts suggest that a "classic history" is nonexistent. The history should give clearly the onset, course, type and distribution of the pain, as well as associated phenomena, such as paresthesias, motor weaknesses and so forth. Statistically, however, there are no symptoms, individual or in the aggregate, that occur with great enough frequency to be considered pathognomonic. In general, the outstanding symptom is pain. This is usually recurrent in the back, with eventual radiation into the posterolateral thigh, the lateral calf and the outer side of the ankle. It is relieved only partially by changes of position, especially those in a direction of spine flexion. Aggravation usually occurs during sneezing or coughing, and is caused by sudden motions, especially those of extension. Paresthesias, when present, are described as numbness or coldness and are not stationary. Motor weaknesses occur in a small percentage of cases and, when present, are continuous. A history of trauma has been reported in from 30 to 60 per cent of cases.

No attempt has been made to separate the symptoms of a bulging unruptured disk from those of a free loose fragment or of a simple unstable disk. This may become important as we learn more about the indications for treatment. At present, so few of the fundamentals regarding the pathogenesis of symptoms are known that only by clarification of these fundamentals can one hope to be more specific.

What has been said about a lack of knowledge to explain symptoms can be applied equally well to the findings on physical examination. In general the lumbar spine is held in flexion and a list is present. Motion of the lumbar spine is limited in all directions, but mainly in extension and lateral bending toward the side of the pain. Straight-leg raising reproduces the pain at a low level. A positive jugular-compression test, paresthesias, muscular weakness and a diminished to absent ankle or knee jerk on the affected side may or may not be present. When the last is present, it strongly suggests the presence of nerve-root pressure. With present understanding of the problem, no one point of history or no one physical finding is pathognomonic of a ruptured disk. A combination of all the facts of the history and all the physical signs should lead the examiner to look for further corroborative evidence, in order to make an accurate diagnosis.

Logically, one looks to x-ray methods for the demonstration of a space-occupying lesion in the spinal canal. Because of the failure of earlier methods, such as air myelography, to be convincing in the majority of cases, substitute methods are being tried. Lipiodol, used according to the method of Kubik,[6] is popular, and most of the oil can be withdrawn by an experienced person. Pantopaque, a thinner oil that maintains a good column, is gaining in popularity as a contrast medium. Substances such as Thorotrast give a less dense shadow, through which midline disks can be visualized,[7] but because of definite dangers, the advantages probably do not exceed the risk of its use. Spurling[8] has been able to localize clinically the level of the protruded disk in 60 per cent of his cases, but in the 40 per cent in which doubt existed, he resorted to the use of Pantopaque. It is well known from surgical exploration that protruded disks are found in cases in which the x-ray films were negative; conversely, protrusions are not always found in cases in which the films were positive. Horwitz[9] has emphasized the discrepancy between x-ray and operative findings. Degenerative disk disease, overgrowths of articular facets and the normal bulging of an overlying ligamentum flavum, by virtue of its anatomic arrangements, are potent causes of defects in the contrast column that can be mistaken for disk fragments. When the contrast medium allows good lateral visualization of the spinal canal, the above-mentioned defects are seen to lie posteriorly and can thereby be more accurately interpreted.

Before leaving the subject of x-ray diagnosis, the value of bone films should be mentioned. Scott[10] has reviewed in detail the radiography of facets, bony overgrowths and fractures, all of which enter into the differential diagnosis. Such films should be a routine part of every back examination.

A narrowed intervertebral space as observed in x-ray films is of no consistent diagnostic value. Vinke and White[11] have conclusively shown that narrowing occurs congenitally, and this condition has been observed frequently as an incidental x-ray finding during examination for symptoms other

than those referable to the spine. Ver Brugghen,[12] in reporting the end results in 66 cases of herniated disk found narrowing of the space in only 30 per cent of the cases. Stump and Narius[13] reported an interesting observation in a patient with meningitis who responded to therapy but who subsequently had severe low-back pain without radiation. X-ray films revealed loss of disk space between the fourth and the fifth lumbar vertebra, without fever to indicate active infection, and the authors concluded that repeated lumbar punctures at that level had entered the interspace and had precipitated a degeneration.

From the foregoing, it is obvious that positive criteria for the diagnosis of a ruptured intervertebral disk are lacking. When the history and examination are suggestive of a protruded disk, bone x-ray films should exclude such possibilities as gross fracture, malignant neoplasm, infection or generalized bone disease. Myelography should be done to show the presence of a space-occupying lesion in the spinal canal, as well as the level or levels of the lesion. An elevated total-protein level in the spinal fluid is helpful, Ver Brugghen[12] having stated that good results from the removal of a ruptured disk can be anticipated in cases in which the total protein is over 40 mg. per 100 cc. The final diagnosis at times can be made only by exploratory laminectomy. This method of diagnosis should be reserved for the cases in which the severity of the pain justifies the operation.

When a diagnosis of ruptured disk has been made, the method of treatment must be selected. End-result study is the only available means of determining the effectiveness of treatment. Sufficient end results have not been reported to draw definite conclusions. Bradford[14] has reviewed the technical advances of operative removal, but stresses a preoperative period of conservative treatment, as does Pilcher.[15] If the pain is intractable and refractory to conservative treatment, this fact in itself has been offered as evidence in favor of the diagnosis of ruptured disk, and also as an indication for operation.

Poppen's[16] technic for removal of the ruptured disk represents the commonly accepted type of hemilaminectomy and extradural approach. Spinal fusion has frequently been combined with the removal of the disk in cases in which there is evidence to suggest instability of the spine. No information is available to intimate the number of cases in which fusion has been done, but it is apparent that such an operation is indicated for continued disability after simple removal of a protrusion.

The final chapter either in the diagnosis or in the treatment of ruptured intervertebral disks has not yet been written. Only by a continued careful analysis of cases and by an honest appraisal of their end results can the data necessary to produce the answer to the present questions be accumulated.

264 Beacon Street

References

1. Mixter, W. J., and Barr, J. S. Rupture of intervertebral disc with involvement of spinal canal. *New Eng. J. Med.* 211:210-215, 1934.
2. Ehrenhaft, J. L. Development of vertebral column as related to certain congenital and pathological changes. *Surg., Gynec. & Obst.* 76:282-292, 1943.
3. Hyndman, O. L., Steindler, A., and Wolkin, J. Herniated intervertebral disk: study of iodized oil column; procaine test in different diagnosis from reflected sciatic pain. *J. A. M. A.* 121:390-401, 1943.
4. Inman, V. T., and Saunders, J. B. Clinico-anatomical aspects of lumbosacral region. *Radiology* 38:669-678, 1942.
5. Young, R., and Brailsford, J. F. Discussion on painful back in soldiers and in industrial workers. *Proc. Roy. Soc. Med.* 36:211-218, 1943.
6. Kubik, C. S., and Hampton, A. O. Removal of iodized oil by lumbar puncture. *New Eng. J. Med.* 224:455-457, 1941.
7. Nosik, W. A. Intraspinal thorotrast. *Am. J. Roentgenol.* 49:214-218, 1943.
8. Spurling, R. G., and Thompson, T. C. Notes on diagnosis of herniated nucleus pulposus in lower lumbar region. *Army M. Bull.* No. 68:142-154, 1943.
9. Horwitz, T. Diagnosis of posterior protrusion of intervertebral disc, with special reference to its differentiation from certain degenerative lesions of disc and its related structures and interpretation of contrast myelography. *Am. J. Roentgenol.* 49:199-213, 1943.
10. Scott, W. G. Low back pain resulting from arthritis and subluxations of apophyseal joints and fractures of articular facets of lumbar spine. *Am. J. Roentgenol.* 48:491-509, 1942.
11. Vinke, I. H., and White, E. H. Congenital narrowing of lumbosacral space. *Surg., Gynec. & Obst.* 76:551-555, 1943.
12. Ver Brugghen, A. H. Herniated nucleus pulposus: report of 75 cases examined and operated on by one observer. *Dis. Nerv. System* 4:165-177, 1943.
13. Stump, J. P., and Narius, S. A. Intervertebral disc injury during spinal puncture. *U. S. Nav. M. Bull.* 41:400-403, 1943.
14. Bradford, F. K. Present status of intervertebral disk problem. *Texas State J. Med.* 38:507-509, 1942.
15. Pilcher, C. Protrusion of nucleus pulposus and other causes of lumbosacral nerve root pain. *J. Missouri M. A.* 39:279-284, 1942.
16. Poppen, J. L. Ruptured intervertebral disk in lumbar and lumbosacral region: technique for removal in uncomplicated case. *S. Clin. North America* 22:865-871, 1942.

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor**

BENJAMIN CASTLEMAN, M.D., *Acting Editor*

EDITH E. PARRIS, *Assistant Editor*

CASE 31051

PRESENTATION OF CASE

A forty-nine-year-old married woman was admitted to the hospital with a palpable mass in the upper abdomen.

The patient had been in good health until three months prior to admission, when she developed a mild ache in the midportion of the back. This was followed in a few hours by a rather diffuse, nonradiating ache in the epigastrium, accompanied by nausea. On one occasion she vomited undigested food recently eaten. There was no hematemesis, jaundice or change in bowel habits, and the stools were of normal appearance. After three days the symptoms completely disappeared. The physician whom she consulted, however, felt a mass in the epigastrium. About two months prior to entry an x-ray examination revealed an "ulcer of the small intestine." At that time the mass was thought to be smaller on palpation. She continued to feel well, with an excellent appetite, and had no recurrence of symptoms, but because of the persistent mass was finally admitted to the hospital for study.

Three years before entry she had undergone a hemorrhoidectomy, with excision of an anal fistula. Her menstrual periods had been regular until five months prior to admission, when she developed amenorrhea, interrupted only by a scanty one-day period about a month before entry.

Physical examination revealed a well-developed and well-nourished woman in no discomfort. The lungs were negative except for some decrease in tactile fremitus over the left apex. The heart was negative. A firm, smooth, nontender, nonpulsating mass was palpable in the epigastrium; it was movable and shifted with respiration. No continuity with any abdominal organ could be demonstrated.

The temperature, pulse and respirations were normal. The blood pressure was 128 systolic, 75 diastolic.

Examination of the blood showed a white-cell count of 8700, with 73 per cent neutrophils, 19 per cent lymphocytes, 7 per cent monocytes and 1 per cent eosinophils. The urine had a specific gravity of 1.020, with a + test for albumin; the sediment contained a few white cells per high-power field. A stool examination was negative. A Hinton test was negative.

A gastrointestinal series revealed an esophagus that was slightly wider than normal. There was no definite evidence of varices. The stomach was rather long and large, and the lesser curvature in the region of the antrum and lower body revealed a large extrinsic pressure defect (Fig. 1). The duodenal cap and second portion of the duodenum were displaced laterally and also showed evidence of extrinsic pressure. A barium enema revealed no abnormalities. An intravenous pyelogram revealed normal kidney outlines, prompt dye excretion and normal urinary passages.

On the seventh hospital day a laparotomy was performed.

DIFFERENTIAL DIAGNOSIS

DR. GEORGE W. HOLMES: Before taking up the x-ray findings in this case I should like to go over the history briefly. I think it is quite important for a radiologist to know something about the history of a patient before he attempts examination, because, unless he does, he is likely to leave out of the examination some of the most significant procedures. I shall therefore approach this case as I think a radiologist should.

The first points of importance are the age of the patient and the duration of the illness. This woman was nearly fifty and she had trouble three months prior to coming into the hospital. There is no reason to suppose that the presenting mass had been there prior to the onset of the symptoms that are described. It was a sudden onset — a mass appeared and all the symptoms disappeared. If it had not been for the mass the patient would not have sought medical advice. The record states that she had an "ulcer of the small intestine." That is a peculiar statement, and I assume that it was made by the patient; a radiologist would probably have specified where the ulcer was. I am inclined to discard the statement as being of no particular value. We should not put too much weight on anything that we have not ourselves observed or proved.

The history also states that she had an anal fistula. I was taught that that can be of tuberculous origin, and to look for tuberculosis elsewhere in the body.

She had amenorrhea, which does not suggest much to me because of her age. I should like to ask Dr. Linton if he would pay any attention to the fact that a woman of this age was not menstruating.

DR. ROBERT R. LINTON: None whatever.

DR. HOLMES: The next point of significance is the character of the mass. On physical examination it was firm, smooth and nontender and did not pulsate; it was movable and shifted with respiration. I consider these observations to be quite important.

*On leave of absence.

The fact that the examiners could not connect it with any particular organ is of little significance.

Among the conditions one has to consider, of course, is an aneurysm. Although pulsation does not prove that a lesion is an aneurysm, the absence of pulsation is of great value. The temperature, pulse, respirations and blood pressure were normal. I should say that it was ruled out by that method and shall not waste any time on it.

In the examination of the gastrointestinal tract there are several significant things. First is the pressure defect on the lesser curvature of the stomach, which extends into the duodenum and seems to lie nearly in the midportion of the abdomen. The

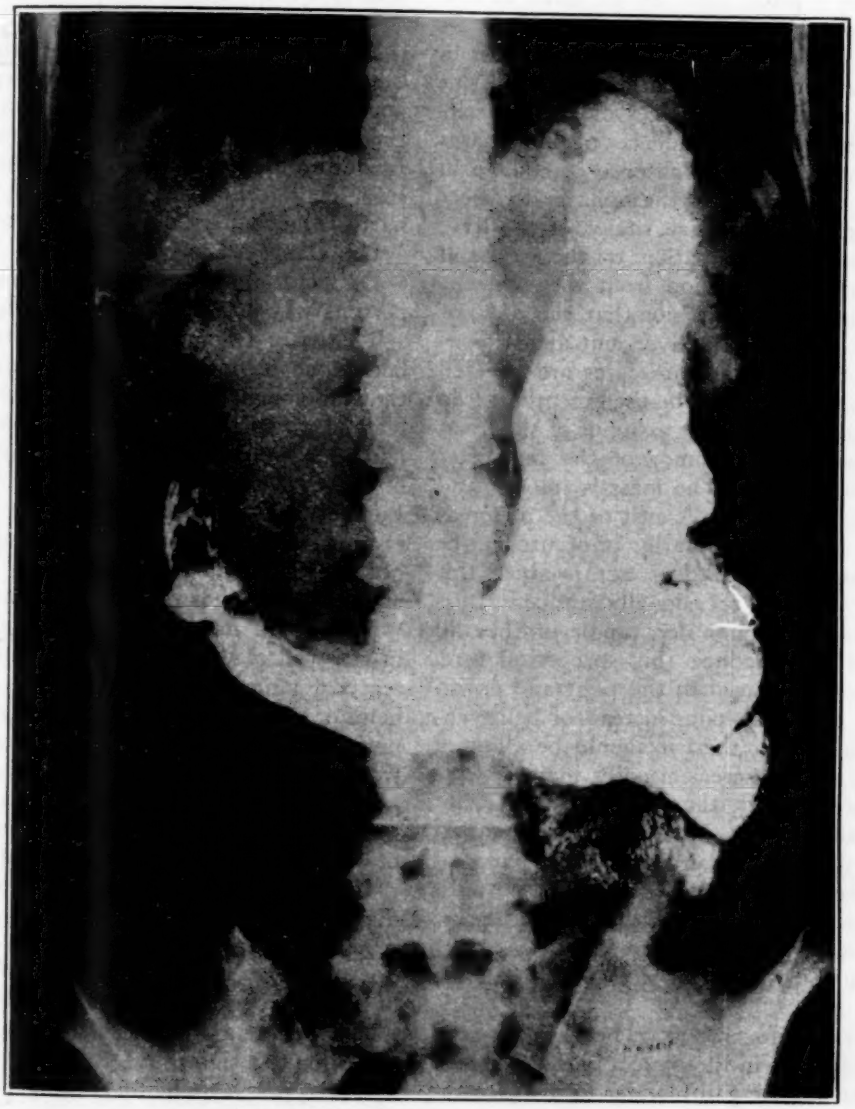


FIGURE 1.

The examination of the blood I also consider to have been within normal limits. Is that true?

DR. LINTON: Yes.

DR. HOLMES: Is there anything in the blood picture to cause a suspicion of lymphoma? That is one of the things that I want to consider.

DR. LINTON: I should think not.

DR. HOLMES: The attending physicians evidently wanted to rule out the urinary tract as a possible source for this mass. Here is the series of films, and density of the shadow is about the same as that of muscle or liver. There is no shadow of diminished or increased density, which would be of some value. I can make out the liver quite well; it is not enlarged or abnormal in shape, and the abstract tells us that the patient had no esophageal varices. There is nothing suggestive in the small or large bowel. The location of the mass is of some importance; it is above the lesser curvature and rather well over toward the midline. I shall go over these points in detail later.

Could this patient have had an abdominal aneurysm? There is no sign of arteriosclerosis. The Hinton test was negative, and the tumor did not pulsate. I believe I can drop that. In considering a case, one should always keep in mind the factors that are of interest to the patient. In this particular case the patient wanted to know if she had a lesion that ought to be operated on, and, if so, whether it was going to be a great risk. So we have to rule out aneurysm on that basis, if on no other.

Could she have had a tumor of the liver? It is in the proper place, and it is smooth, round and not lobulated, but she had no varices or signs of cirrhosis; also, there is no evidence of metastases elsewhere in the body. The absence of change in the liver and the absence of esophageal varices make the diagnosis of primary tumor of the liver unlikely. If I had seen this patient on the ward and was making my interpretation from the evidence that we have here, I should say that she did not have a primary tumor of the liver, but at this conference, where many of the rare cases are selected for discussion, this case might be the exception; I do not believe that I can rule out a tumor of the liver.

Could it have been a tumor of the pancreas? It might well have been. The mass is smooth and round and probably cystic. A cyst of the pancreas is not too infrequent. Ordinarily it occurs in the head of the pancreas and does not produce this type of deformity; but occasionally it does. It is not particularly uncommon for tumor in the tail of the pancreas to produce this sort of picture. The duodenum is displaced to the right and downward, and the duodenal loop, instead of being enlarged, is much smaller than it should be. Tumor of the head of the pancreas usually increases the size of the loop rather than diminishes it, but tumor of the tail may not. Therefore, I believe that that is a likely diagnosis. Can tumor of the pancreas cause as few symptoms as this patient had? And is it consistent with the symptoms that she did have? Can you help me on that, Dr. Sweet?

Dr. Richard H. Sweet: If it were a cyst, I should think so.

Dr. Holmes: Could this have been hydrops of the gall bladder? It is in the correct place. I should expect a hydrops of the gall bladder to displace the whole duodenum downward, but it looks a little too far to the left. But I do not see how I can rule that out on the evidence that we have. Could one have hydrops of the gall bladder with absence of symptoms?

Dr. Sweet: I doubt it.

Dr. Holmes: I hope that Dr. Sweet and Dr. Linton are helping me. I have been accused of not helping the surgeons at times.

Could it have been a lymphoma? Lymphomatous masses or a single mass does occur in the belly. Was a careful search made for enlarged lymph nodes elsewhere in the body?

Dr. Benjamin Castleman: None were found.

Dr. Holmes: The blood picture was normal. Furthermore, a lymphoma usually is not so round as this mass; it is apt to be lobular. I am going to rule it out on that basis.

On account of the anal fistula, I have to think of tuberculous nodes. There is no calcification in the tumor, and no other calcified nodes are seen elsewhere. I believe that we can rule it out.

We come down to some form of cyst — a cyst in the lesser omentum, a cyst of the pancreas, a dermoid cyst or an echinococcal cyst. Dermoid and echinococcal cysts are likely to contain calcium, but there is no evidence of calcification in this tumor. In addition, the appearance of the lesion and the story make echinococcal cyst seem unlikely. What part of the country did the patient come from?

Dr. Castleman: New England.

Dr. Holmes: Echinococcal cysts are rare in persons who have not been outside New England.

There are two or three things that should have been done during the x-ray examination, provided the radiologist had all the facts that I have. For instance, if this were a dermoid cyst and the patient had a film taken in the upright position, the contents of the cyst might have settled in different layers. Furthermore, there should have been an x-ray examination of the chest to be sure that she did not have metastases. That would help in deciding whether the tumor was benign or malignant.

This could have been a leiomyosarcoma arising in the wall of the stomach. In that case, a careful search for metastases in the lung would have been helpful, as well as an examination in the upright position to see whether the mass could be separated from the stomach. A leiomyosarcoma would be adherent to the stomach, whereas a cyst in the pancreas would not. They may have done all this, of course; but there is no record of it.

In conclusion I shall make the most obvious diagnosis, that is, a cyst, probably in the tail of the pancreas. I cannot be absolutely certain that it was not a primary tumor of the liver, but in the absence of cirrhosis of the liver this is extremely rare.

Dr. Arthur W. Allen: I should like to call attention to a sign that Dr. Lincoln Davis discovered several years ago in diagnosing echinococcal cyst. He found that on percussion it gave the same sensation that one would get on percussing an innerspring mattress. This abstract says nothing about percussion, and that might have helped to rule out one possibility.

Dr. Sweet: I did not percuss it.

Dr. Allen: Another interesting feature is that the mass was described as movable and shifting with respiration. It does not say how movable; that would be helpful in differential diagnosis because cysts arising in the mesentery are quite movable.

Dr. Holmes: Would a cyst in the lesser omentum be movable?

DR. ALLEN: Yes; a great deal more so than a pancreatic cyst, which would move only with respiration.

DR. SWEET: This was not so movable as one would expect for a mesenteric cyst; nor did it move so much as the one large hepatoma of the liver that I happened to have had and that was presented here two or three years ago.[1]

DR. HOLMES: If this was a mesenteric cyst it must have been in the lesser omentum. I do not believe that a cyst in the greater omentum or in the mesentery of the bowel could have produced such an extensive pressure defect in the stomach.

CLINICAL DIAGNOSIS

Tumor of liver ?
Cyst of pancreas ?

DR. HOLMES'S DIAGNOSIS

Cyst, probably in tail of pancreas.

ANATOMICAL DIAGNOSIS

Islet-cell adenoma of pancreas.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: Will you tell us about your operative findings, Dr. Sweet?

DR. SWEET: I should like to say first that Dr. Holmes certainly made an excellent clinical analysis of this case, far better than we did. I decided that it must be a tumor of either the liver or the pancreas. At operation the mass was obviously in the pancreas. It moved with the pancreas the way a carcinoma of the stomach does when it is adherent to the pancreas. The tumor was not pedunculated and could be moved only by moving the entire pancreas; it was part of the body of the pancreas, being located just to the left of the head, close to the duodenum. It was vascular and appeared to be a solid tumor or, if a cyst, an extremely tense one. It was somewhat of a technical stunt to get it off the middle colic vessels without destroying the vascular supply of the duodenum, but it came out, leaving a great hollow in the pancreas. I had never seen anything like it before.

DR. CASTLEMAN: As Dr. Sweet indicated, the specimen we received was circumscribed, with a fairly smooth surface. It was distinctly brownish and, on section, soft and not at all cystic. Microscopic examination showed it to be an adenoma of the islet cells of the pancreas, which apparently had not produced any endocrine disturbance. We went back and questioned the patient about hypoglycemic spells but were unable to elicit any suggestion of one. In Whipple's[2] review of these tumors, he found that the number that were asymptomatic was greater than that of those producing hypoglycemic symptoms.

DR. HOLMES: Was there any evidence of hemorrhage into the tumor?

DR. CASTLEMAN: No.

REFERENCES

1. Case records of the Massachusetts General Hospital (Case 29331). *New Eng. J. Med.* **229**:342-345, 1943.
2. Whipple, A. O. Hyperinsulinism. *Nelson's New Loose-Leaf Surgery.* Vol. V, Chap. XII. New York: Thomas Nelson & Sons, 1935. Pp. 613-636.

CASE 31052

PRESENTATION OF CASE

A thirty-one-year-old married woman was admitted to the hospital with abdominal cramps.

One month prior to admission the patient missed her expected menstrual period. Four to five days later she began to have vaginal bleeding, passing fresh blood and dark shreds on the first day, followed by intermittent spotting. Her breasts had enlarged and were tender. Twenty-four hours before entry she developed severe cramps in the upper portion of the abdomen. These were quite severe during the night and interfered with sleep. There was no nausea, vomiting, chills, fever or diarrhea. She had had a normal bowel movement on the day prior to admission but none since.

The patient had been admitted to the hospital ten years previously with abdominal cramps. A laparotomy performed at that time revealed a third degree retroversion of the uterus and chronic typhlitis. A ventral suspension of the uterus was done, and the appendix was removed.

She had been married two other times, followed by divorce. During her first marriage eight years previously she had one pregnancy, which was aborted. There were no other pregnancies.

Physical examination on admission revealed a well-developed and well-nourished young woman. The breasts were moderately enlarged and tender, with a widened areola. The heart and lungs were negative. The abdomen revealed diffuse tenderness without spasm but with moderate rebound tenderness in both lower quadrants. No masses were felt. Peristalsis was normal. Pelvic examination revealed a soft uterus of normal size. The fundus was in anterior position and freely movable. The cervix was moderately soft. An irregular, slightly tender mass, 3 to 4 cm. in diameter, was felt in the right adnexal region.

The temperature was 99.8°F., the pulse 66, and the respirations 20. The blood pressure was 110 systolic, 56 diastolic.

Examination of the blood revealed a white-cell count of 13,500. The hemoglobin was 11.8 gm. The urine was essentially negative. A stool examination was negative. A Friedman test for pregnancy was positive.

A roentgenogram of the abdomen revealed an unusual distribution of gas, there being a consider-

able amount in the transverse and descending colon but little in the small bowel and stomach.

On the eighth hospital day an operation was performed.

Differential Diagnosis

Dr. Francis M. Ingersoll: As I start my discussion there is one premise that I think I shall have to assume, namely, that this patient was pregnant. Certain facts pointing toward it cannot be refuted. The history is compatible. She had a positive Friedman test, and the physical examination also bears out that diagnosis. There are two things that bothered me after reading the case report and that did not seem to fit in with anything that I could think of as a diagnosis. One was that at the time of admission she had severe cramps in the upper abdomen. In my experience that does not fit in with any condition in the pelvis related to a normal pregnancy. The other thing was that I cannot explain the x-ray findings on the basis of pregnancy.

Dr. Benjamin Castleman: Dr. Holmes's comment was that reversed peristalsis of the colon at the time the films were taken might have produced such an appearance.

Dr. Ingersoll: Then from the x-ray examination I believe that I shall have to rule out any lesion in the small or large bowel.

The differential diagnosis concerns whether the patient had an extrauterine pregnancy or an intrauterine pregnancy with a threatened miscarriage or an incomplete abortion. Extrauterine pregnancies are relatively frequent, 1 out of every 300 gravid women having one. The setup here is excellent for an ectopic pregnancy. This woman had been married three times and had had one abortion and possibly pelvic inflammatory disease, all of which is an excellent cause for an extrauterine pregnancy. So the first possibility that comes to me is that this mass that was felt in the abdomen was due to an ectopic pregnancy, possibly in the tube. It might have been one of the rare pregnancies that occur in the ovary, the ovum being fertilized just as it is discharged from the ovary, with implantation taking place there. It is possible that the patient had a tubal abortion at the time of the severe pain and that the ovum was outside the tube and actually attached to the large bowel, irritating it and causing a reflux of gas back into the transverse colon, as Dr. Holmes described.

The possibilities other than extrauterine pregnancy are those associated with an incomplete miscarriage. For example, she could have had an incomplete miscarriage to account for the way the uterus felt, and the mass that was felt on the right side could have been inflammatory, — a tubo-ovarian abscess, — although it is quite rare to have a patient with both pregnancy and a real abscess in the tube and ovary. The right-sided mass might have been an endometrioma; she was thirty-one years of age and had never had a full-term pregnancy. The other thing that occurred to me is that this patient might have had a normal intrauterine pregnancy together with a small cyst of the ovary that had twisted, thus destroying the corpus luteum and producing a miscarriage.

In summary, I shall say that the patient was pregnant and that either the pregnancy was ectopic or she had an incomplete miscarriage, with some other associated phenomenon. If I had to commit myself to one diagnosis, it seems to me that this whole case fits in best with an extrauterine pregnancy, and since this is a clinicopathologic case, in which one expects the unusual, I shall postulate that the extrauterine pregnancy was implanted on the ovary.

Dr. Fred A. Simmons: The patient was sent to me by an obstetrician because of sterility; she had been married to her third husband for three years. The first time that I examined her, there was a mass on the right side, but it did not change in the subsequent five or six weeks. It took a long time to convince me that it was a tubal pregnancy. At the first visit to the office her menstrual period was a day or two overdue and I assumed that she was pregnant. Following amenorrhea for eight or ten days she then started to flow. Since I thought it was a normal pregnancy, I tried to maintain it by bedrest and so forth. Then when she developed cramps, I sent her into the hospital.

On the fourth hospital day she passed a piece of tissue 1 cm. wide and 4 cm. long, which I immediately assumed was produced by conception. It was sent to the laboratory, where a diagnosis of decidua without chorionic villi was made, which means ectopic pregnancy.

Clinical Diagnosis

Tubal pregnancy.

Dr. Ingersoll's Diagnosis

Ectopic pregnancy, possibly in ovary.

Anatomical Diagnoses

Tubal pregnancy.
Salpingitis isthmica nodosa, bilateral.

Pathological Discussion

Dr. Simmons: The patient was operated on, and we found a tubal pregnancy on the right. She had in addition a lesion in the isthmic portion of both tubes that grossly suggested salpingitis isthmica nodosa.

Dr. Castleman: How much blood did she have in the peritoneal cavity?

Dr. Simmons: About 40 cc.

Dr. Castleman: One interesting point, which Dr. Simmons mentioned, is the presence of decidua in the uterus in cases of ectopic pregnancy. In this

case the decidua was so abundant that we seriously considered a diagnosis of uterine pregnancy. The absence of any trace of a chorionic villus, however, should make one suspect some sort of ectopic pregnancy.

In the gross specimen there were, as Dr. Simmons has stated, fibrous nodules near the cornua of the uterus — a condition that has been called "salpingitis isthmica nodosa." On microscopic examination there were islands of epithelium in gland formation, although they were probably not true glands but pseudoglands. The ordinary explanation of this condition is that some inflammatory process has occurred in the fallopian tube with the formation of a great deal of connective tissue, which pinches off the tortuous epithelial folds, so that they appear as acini in the walls of the tube. Perhaps that is the best explanation for most of these cases. In a recent paper, however, Schenken and Burns,[1] who made serial sections of the entire tube, state that they believe that these little islands of epithelium are not entirely the result of infection but often due to diverticulosis of the tube, with or without inflammation.

Another explanation of salpingitis isthmica nodosa is that it is endometriosis of the fallopian tube. The glands are similar to the endometrium, but there is no stroma present and most of these patients do not have endometriosis elsewhere.

DR. SIMMONS: It is difficult for me to conceive how this patient could have become pregnant, although Dr. Meigs[2] has described one case of pregnancy in a patient with bilateral salpingitis isthmica nodosa. It must be extremely rare. In most textbooks of gynecology the lesion is described as being due to gonorrhea, tuberculosis or adenomyosis.

DR. CASTLEMAN: Those are the usually accepted causes, but the suggestion of Schenken and Burns that it may be due to diverticulosis is intriguing.

REFERENCES

1. Schenken, J. R., and Burns, E. L. Study and classification of nodular lesions of fallopian tubes: "salpingitis isthmica nodosa." *Am. J Obst. & Gynec.* 45:624-636, 1943.
2. Meigs, J. V. *Tumors of the Female Pelvic Organs.* 533 pp. New York: Macmillan Company, 1934. P. 358.

The New England
Journal of Medicine

Formerly
The Boston Medical and Surgical Journal
Established 1828

Owned by the Massachusetts Medical Society and Published under the Jurisdiction of the Committee on Publications

Richard M. Smith, M.D., *Chairman*
James P. O'Hare, M.D. Conrad Wesselhoeft, M.D.
Oliver Cope, M.D. John Fallon, M.D.

Official Organ of
The Massachusetts Medical Society
and
The New Hampshire Medical Society

Editorial Board
Joseph Garland, M.D. Charles C. Lund, M.D.
Shields Warren, M.D. A. Warren Stearns, M.D.
C. Guy Lane, M.D. Dwight O'Hara, M.D.
William A. Rogers, M.D. Chester S. Keefer, M.D.
Stephen Rushmore, M.D. Fletcher H. Colby, M.D.
Henry R. Viets, M.D. Robert L. Goodale, M.D.
Robert M. Green, M.D. Chester M. Jones, M.D.
Harvey R. Morrison, M.D.
Associate Editors
Thomas H. Lanman, M.D. Donald Munro, M.D.
Henry Jackson, Jr., M.D.
Walter P. Bowers, M.D., Editor Emeritus
Robert N. Nye, M.D., Managing Editor
Clara D. Davies, Assistant Editor

Subscription Terms: $6.00 per year in advance, postage paid, for the United States (medical students, $3.50 per year); Canada, $7.04 per year (Boston funds); $8.52 per year for all foreign countries belonging to the Postal Union.

Material should be received not later than noon on Thursday, two weeks before date of publication.

The Journal does not hold itself responsible for statements made by any contributor.

Communications should be addressed to the *New England Journal of Medicine*, 8 Fenway, Boston 15, Massachusetts.

STANDARDS OF MEDICAL EDUCATION

On January 5, 1945, the failure of the Massachusetts Approving Authority to accredit the Middlesex University School of Medicine was upheld by the Superior Court of Suffolk County.

The law establishing the Approving Authority was signed by the Governor of Massachusetts, James M. Curley, in 1936. A photograph taken at the time he signed the bill shows several members of the Massachusetts Medical Society watching the proceedings with great interest, among them being Dr. Charles E. Mongan, who at that time was president of the Society and had much to do with the campaign to enact the legislation. Also in the group was the present dean of the Middlesex University School of Medicine, Dr. Stephen Rushmore, who then was secretary of the Board of Registration in Medicine and automatically became a member of the Approving Authority.

Soon after its establishment, the Approving Authority drew up the seventeen qualifications that a medical school must meet in order to be approved. These qualifications are the same as those used to measure the quality of the schools that have recently applied for approval, and it was the failure of the Middlesex University School of Medicine to meet all the qualifications that made it necessary for the present Approving Authority to deny approval. This denial followed three inspections by three different groups comprising the Approving Authority and a public hearing held in July, 1944.

The law passed in 1936 stated that students who matriculated at a medical school on or after January 1, 1939, must graduate from a school accredited by the Approving Authority in order to be eligible to take the examination for registration in this state. The law was amended in 1939, the effective date being changed to January 1, 1941. Students coming under this classification began to graduate from medical schools during the summer of 1944, and those who had received their diplomas from schools not approved by the Approving Authority have been denied the right of examination by the Board of Registration in Medicine. Massachusetts has three such schools, namely, the Middlesex University School of Medicine, the Massachusetts College of Osteopathy and the College of Physicians and Surgeons. The last two have never asked for approval.

At long last the practice of medicine in the Commonwealth is open only to those men and women who have been properly trained, and Massachusetts need no longer be called "the dumping ground" for medical-school graduates; but a number of bills that aim either to abolish the Approving Authority or to postpone again the date of its effectiveness have already been introduced for the consideration of the present session of the General Court. The passage of such legislation can either halt or stop forever the progress toward higher medical standards, and high standards of medical education *must* be maintained in these days when the practice of

medicine is being subjected to criticism. Every member of the Massachusetts Medical Society should do all within his power in an attempt to bring about the defeat of these bills.

A NEW AND RAPID LABORATORY TEST FOR SMALLPOX

Major van Rooyen and Major Illingworth,[1] of the Royal Army Medical Corps, have recently contributed what appears to be a most valuable laboratory test for smallpox. According to them, a smear preparation from a suspected case of smallpox can be made, stained and examined and the report handed to the physician in half an hour. The material is obtained by delicately scraping either the base of a vesicle or, still better, an early papule without drawing blood. This is rubbed onto a specially prepared slide, stained according to the Paschen method (which is described in detail) and examined under the microscope. If the material was secured from a case of smallpox, the trained eye quickly detects masses of characteristic elementary bodies. Not only are these infinitely more numerous than the elementary bodies found in chicken pox[2] but they are about twice as large. The authors warn that this method applies only to the identification of smallpox bodies and is not applicable to those of chicken pox, since the latter are too scanty.

The test was positive in 77 cases of smallpox and negative in only 3. In no case did a positive test disagree with the clinical diagnosis. The test proved particularly valuable in the early diagnosis of cases of modified smallpox, in which only a few discrete lesions, suggestive of chicken pox, were present and also in the early stages of the severe forms of hemorrhagic smallpox in which the papular stage suggested typhus fever or measles. Indeed, in the latter type of case the earliest buccal lesions often resembled Koplik spots. The importance of this test can best be appreciated by realizing that the Paul test, in which infective material is scratched into a rabbit's cornea, can only be completed in three days and that the same applies to the chick chorioallontoic-membrane test, whereas the flocculation test is not reliable until after the first week of the disease.

In another contribution Major Illingworth and Major Oliver[3] report their observations on an epidemic of smallpox in Egypt during 1943 and 1944. These authors emphasize that the early clinical differentiation of smallpox and chicken pox was often impossible. Not only was the typical distribution of the lesions ("centrifugal" and "centripetal," respectively) a snare and a delusion, but they also found that smallpox lesions came out in crops over a period of four or five days, a characteristic usually ascribed to the lesions of chicken pox, and that maturation of the lesions was sometimes quite as rapid in smallpox as in chicken pox. They noted oval lesions in the folds of the skin and petechiae in the axillas in cases of the hemorrhagic type. Even the characteristic backache of the prodromal stage of smallpox was by no means a prominent symptom. Finally, 96 of the 100 patients in the series had been previously vaccinated, 70 having been vaccinated "successfully" within two years.

All this goes to show that there are exceptions to every point of differentiation between smallpox and chicken pox, as was brought out in a recent progress review in the *Journal*.[4] Smallpox varies in character and severity in different localities. Under wartime conditions as they exist today in Egypt, with the influx of troops from so many parts of the world, this disease in almost every hue of human skin presents extraordinary difficulties. Faced with these, the authors found that examination of the scrapings from papules or vesicles for elementary bodies was of the greatest assistance in making an early diagnosis.

References

1. van Rooyen, C. E., and Illingworth, R. S. Laboratory test for diagnosis of smallpox. *Brit. M. J.* 2:526-529, 1944.
2. Tyzzer, E. E. Histology of skin lesions in varicella. *Philippine J. Sc.* 1:349-372, 1906.
3. Illingworth, R. S., and Oliver, W. A. Smallpox in Middle East. *Lancet* 247:681-685, 1944.
4. Wesselhoeft, C. Differential diagnosis of chicken pox and smallpox. *New Eng. J. Med.* 230:15-19, 1944.

MASSACHUSETTS MEDICAL SOCIETY

DEATH

HERBERT — Edward Herbert, M.D., of Fall River, died June 26. He was in his seventieth year.

Dr. Herbert received his degree from Columbia University College of Physicians and Surgeons, New York, in 1902. He was a fellow of the American Medical Association.

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

COMMUNICABLE DISEASES IN MASSACHUSETTS FOR DECEMBER, 1944

RÉSUMÉ

Diseases	December 1944	December 1943	Seven-Year Median
Anterior poliomyelitis	11	14	2
Chancroid	5	0	*
Chicken pox	1407	1618	1603
Diphtheria	29	32	19
Dog bite	517	431	561
Dysentery, bacillary	12	105	16
German measles	89	118	68
Gonorrhea	373	477	335
Granuloma inguinale	5	0	*
Lymphogranuloma venereum	2	0	*
Malaria	42	11	0
Measles	235	1320	1082
Meningitis, meningococcal	26	60	7
Meningitis, Pfeiffer-bacillus	7	3	2
Meningitis, pneumococcal	9	7	†
Meningitis, staphylococcal	—	—	†
Meningitis, streptococcal	—	1	†
Meningitis, other forms	1	4	†
Meningitis, undetermined	1	5	†
Mumps	1353	670	597
Pneumonia, lobar	233	576	407
Salmonella infections	5	5	4
Scarlet fever	1052	978	926
Syphilis	373	560	475
Tuberculosis, pulmonary	174	194	241
Tuberculosis, other forms	12	18	26
Typhoid fever	6	2	5
Undulant fever	3	3	3
Whooping cough	466	341	784

*Made reportable in December, 1943.

†Pfeiffer-bacillus meningitis only other form reportable previous to 1941.

COMMENT

Diphtheria continues at a relatively high level — approximately at one and a half times the seven-year median. This indicates, of course, that local immunization effort should be stepped up.

Mumps continues its gradual climb toward higher levels, and scarlet fever is again on the increase after a few months of lower prevalence. Measles and lobar pneumonia, on the other hand, have dropped to almost record low levels.

Malaria is now regularly appearing in the reports of certain boards of health, but this is due to the presence in Massachusetts of service men and others who have acquired the disease in foreign service.

GEOGRAPHICAL DISTRIBUTION OF CERTAIN DISEASES

Anterior poliomyelitis was reported from: Arlington, 1; Boston, 3; Hadley, 1; Holyoke, 1; Newton, 1; Oxford, 1; Waltham, 1; Wellesley, 1; West Springfield, 1; total, 11.

Diphtheria was reported from: Barnstable, 4; Boston, 6; Bourne, 1; Falmouth, 1; Lowell, 1; Medford, 1; New Bedford, 4; Rockland, 1; Salem, 1; Somerville, 7; Wakefield, 1; Weymouth, 1; total, 29.

Dysentery, bacillary, was reported from: Amherst, 2; Everett, 1; Lowell, 1; Malden, 4; Medford, 2; Northampton, 1; Quincy, 1; total, 12.

Encephalitis, infectious, was reported from: Medford, 1; Winchendon, 1; total, 2.

Malaria was reported from: Amesbury, 1; Camp Edwards, 9; Cushing General Hospital, 3; Dedham, 1; Easton, 1; Everett, 1; Hardwick, 1; Haverhill, 2; Ipswich, 1; Marlboro, 1; Newton, 2; Quincy, 1; Regional Hospital, Waltham, 16; Somerville, 1; Stoneham, 1; total, 42.

Meningitis, meningococcal, was reported from: Arlington, 1; Attleboro, 1; Boston, 8; Bridgewater, 1; Fall River, 2; Framingham, 1; Gloucester, 1; Haverhill, 1; Lawrence, 1; Lynn, 1; Malden, 1; Medford, 1; Melrose, 1; Newton, 1; Saugus, 1; Somerville, 1; Weymouth, 1; Worcester, 1; total 26.

Meningitis, Pfeiffer-bacillus, was reported from: Arlington, 1; Boston, 2; Cambridge, 1; Hanson, 1; Medford, 1; Watertown, 1; total, 7.

Meningitis, pneumococcal, was reported from: Boston, 1; Brockton, 1; Chicopee, 1; Lawrence, 1; Lynn, 1; Marion, 1; Medford, 1; Springfield, 1; Westport, 1; total, 9.

Meningitis, other forms, was reported from: Boston, 1; total, 1.

Meningitis, undetermined, was reported from: Boston, 1; total, 1.

Salmonella infections were reported from: Lawrence, 2; North Andover, 1; Somerville, 1; Southbridge, 1; total, 5.

Septic sore throat was reported from: Avon, 2; Belmont, 1; Boston, 14; Marion, 1; Medford, 1; Merrimac, 1; Revere, 1; total, 21.

Tetanus was reported from: Medway, 1; total, 1.

Trachoma was reported from: Lee, 1; Watertown, 1; total, 2.

Trichinosis was reported from: Boston, 4; total, 4.

Typhoid fever was reported from: Boston, 2; Haverhill, 1; Lawrence, 1; Tewksbury, 1; Warren, 1; total, 6.

Typhus fever was reported from: Boston, 1; total, 1.

Undulant fever was reported from: Boston, 1; Bourne, 1; Sheffield, 1; total, 3.

CONSULTATION CLINICS FOR CRIPPLED CHILDREN IN MASSACHUSETTS UNDER THE PROVISIONS OF THE SOCIAL SECURITY ACT

Clinic	Date	Clinic Consultant
Lowell	February 2	Albert H. Brewster
Salem	February 5	Paul W. Hugenberger
Haverhill	February 7	William T. Green
Brockton	February 8	George W. Van Gorder
Worcester	February 16	John W. O'Meara
Pittsfield	February 19	Frank A. Slowick
Springfield	February 21	Garry deN. Hough, Jr.
Fall River	February 26	Eugene A. McCarthy
Hyannis	February 27	Paul L. Norton

NOTICES

JOSEPH H. PRATT DIAGNOSTIC HOSPITAL

Bennet Street, Boston
Lecture Hall, 9–10 a.m.

MEDICAL CONFERENCE PROGRAM

Friday, February 2 — Medical Disorders in Pregnancy. Dr. Lewis Dexter.

Tuesday, February 6 — Neuro-Hormonal Factors in the Origin and Treatment of Cardiovascular Disease. Dr. W. Raab.

Wednesday, February 7 — My Recent Trip to the West Indies. Dr. William Dameshek.

Friday, February 9 — Erythrocyte Preservation. Dr. Joseph F. Ross.

Wednesday, February 14 — Bronchiectasis: Medical and surgical aspects. Dr. Bert Cotton.

Friday, February 16 — Dwarfism. Dr. Nathan Talbot.

Wednesday, February 21 — Interesting Effects on Lungs and Air Passages of Breathing Extremely Hot or Cold Air. Dr. Alan R. Moritz.

Friday, February 23 — Protein Nutrition in Problems of Medical Interest. Dr. Fredrick J. Stare.

Wednesday, February 28 — Penicillin in Venereal Disease. Dr. Oscar F. Cox.

On Monday mornings clinics will be given by Dr. Samuel Proger. On Saturday mornings clinics will be given by Dr. William Dameshek. On Tuesday and Thursday mornings Dr. S. J. Thannhauser will give medical clinics on hospital cases.

MASSACHUSETTS PHYSIOTHERAPY ASSOCIATION

The next meeting of the Massachusetts Physiotherapy Association will be held at the Women's Educational and Industrial Union on Tuesday, February 6. At 7:00 p.m., following a dinner and business meeting, Miss Margaret Arey, supervising instructor in public-health nursing in orthopedics in Massachusetts, will talk on the subject "The Care of Patients with Amputations."

HARVARD MEDICAL SOCIETY

A meeting of the Harvard Medical Society will be held in the amphitheater of the Peter Bent Brigham Hospital on Tuesday, February 13, at 8:15 p.m.

PROGRAM

Clinical case presentation from the Boston City Hospital.

The Distribution of Lipids in Blood Cells and Plasma. Drs. F. F. Foldes and A. J. Murphy.

Histochemical Studies of the Retina. Dr. C. B. Anfinsen.

Studies on Recently Isolated Influenza Viruses. Drs. J. F. Enders, M. Finland, E. G. Mills and M. W. Barnes.

(*Notices continued on page xix*)

NOTICES (*Continued from page 148*)

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING THURSDAY, FEBRUARY 8

FRIDAY, FEBRUARY 9

10:50 a.m. Local Therapy. Dr. E. Lafreniere. (Postgraduate clinic in dermatology and syphilology.) Amphitheater, Mallory Building, Boston City Hospital.

SATURDAY, FEBRUARY 10

*10:00 a.m.–12:00 m. Medical staff rounds. Peter Bent Brigham Hospital.

MONDAY, FEBRUARY 12

*12:00 m.–1:00 p.m. Clinicopathological conference. Peter Bent Brigham Hospital.

TUESDAY, FEBRUARY 13

*12:15–1:15 p.m. Clinicoroentgenological conference. Peter Bent Brigham Hospital.

WEDNESDAY, FEBRUARY 14

*12:00 m. Clinicopathological conference. Children's Hospital.
7:15 p.m. Graduate seminar in pediatrics. Children's Medical Service. Amphitheater 3A, Massachusetts General Hospital.

*Open to the medical profession.

FEBRUARY 2-28. Joseph H. Pratt Diagnostic Hospital. Medical conference program. Page 148.

FEBRUARY 3. American Board of Obstetrics and Gynecology. Page 696, issue of November 16.

FEBRUARY 6. Massachusetts Physiotherapy Association. Page 148.

FEBRUARY 8. Surgery Connected with the Liver and Pancreas. Dr. Joseph Tartakoff. Pentucket Association of Physicians. 8:30 p.m. Haverhill.

FEBRUARY 11. National Conference on Medical Service. Page 30, issue of January 4.

FEBRUARY 13. Harvard Medical Society. Page 148.

FEBRUARY 19. American Board of Internal Medicine. Page 436, issue of September 21.

FEBRUARY 28. Tufts Medical Alumni Lecture. Tufts College Medical School. 4:00 p.m.

APRIL 30. New York Institute of Clinical Oral Pathology. Page 120, issue of January 25.

MAY 22-24. Hotel Statler, Boston. Annual meeting of the Massachusetts Medical Society.

SEPTEMBER 17. American Public Health Association. Page 752, issue of November 30.

DISTRICT MEDICAL SOCIETIES

PLYMOUTH

FEBRUARY 15. Jordan Hospital, Plymouth.
MARCH 15. Goddard Hospital, Brockton.
APRIL 26. Toll House, Whitman.
MAY 17. Lakeville Sanatorium, Lakeville.

All meetings will be held at 11 a.m.

WORCESTER

FEBRUARY 14. Worcester State Hospital.
MARCH 14. Worcester Memorial Hospital.
APRIL 11. Hahnemann Hospital, Worcester.
MAY 9. Annual meeting.

A Leading Economist Says:

"Every successful business man today realizes that advertising is absolutely essential. Moreover, efficient advertising is an economic asset and not a waste, as some consumers seem to think. Instead of increasing prices it really has lowered them. This comes about through the economies of mass production, an American Business development that would have been impossible without advertising." — *Boston Better Business Bureau.*

Channing Sanitarium

ESTABLISHED 1879

A pleasant country community of cottages built for the homelike care and treatment of nervous patients. Electroshock therapy to selected cases.

Occupational therapy. Tennis court. Sports building.

JACKSON M. THOMAS, M.D., *Superintendent* CLIFFORD G. ROUNSEFELL, M.D., *Resident Physician*

WELLESLEY, MASSACHUSETTS

Telephone — Wellesley 0464

BREAST MILK

may be obtained at the offices and laboratory of

The Directory for Mothers' Milk

Incorporated

221 Longwood Avenue, Boston
Telephone BEA 5330

Prices will be adjusted to make the milk available to all who need it

Sent packed in ice to all parts of New England

Bournewood Hospital

300 SOUTH STREET, BROOKLINE, MASS.

Established 1884

For a limited number of cases of mental and nervous diseases

POST OFFICE, CHESTNUT HILL

Telephone PAR 0300

GEORGE H. TORNEY, M.D.

Washingtonian Hospital

41 WALTHAM STREET, BOSTON, MASS.
Founded 1841
A non-profit-making, endowed institution reorganized, for the
MODERN TREATMENT OF MEN SUFFERING FROM ACUTE OR CHRONIC

ALCOHOLISM

JOSEPH THIMANN, M.D., *Medical Superintendent*
MERRILL MOORE, M.D., *Director of Research*

Visits by Psychiatric and Neurological Staff
Consultants in Medicine, Surgery and the Specialties
Rates Moderate
For information: consult the Medical Superintendent
Telephones: HAN 1750 and 1751

$34,000.00
IN WAR BONDS AS PRIZES

For the best art works memorializing the medical profession's

"Courage and Devotion Beyond the Call of Duty"

(In War and in Peace)

42 PRIZES

21 OF THE 42 PRIZES ARE RESERVED FOR MEDICAL OFFICERS OF THE ARMED FORCES. THE OTHER 21 PRIZES ARE FOR CIVILIAN PHYSICIANS

The American Physicians Art Association, through the cooperation of Mead Johnson & Company, announces the following Prize Contest:

1. **SUBJECT:** "Courage and Devotion Beyond the Call of Duty" — on the part of members of the medical profession — in military or civilian practice. Any contestant may portray either the military or civilian aspect of the subject (or both, if shown in one piece).

2. **MEDIA:** The physician-artist's choice of one of the following:

   1. PAINTING in oil or egg tempera.
   2. WATER COLOR, transparent or opaque.
   3. SCULPTURE in any medium.
   4. DRAWING in any medium.
   5. PRINTS, including etching, engraving, lithography, wood block and linoleum block (on paper or cloth).
   6. PHOTOGRAPHY, including bromoil, tinted and kodachrome, as well as photo-montage.

   SUGGESTIONS: COMPLETE SKETCHES FOR MURAL DECORATIONS: In oil, egg tempera or water color drawing; PHOTO MURAL; BAS RELIEF SCULPTURE: are all eligible.

3. **ELIGIBILITY — See Footnote ★**

4. **DEFINITION — See Footnote ★**

5. **PRIZES: Forty-two prizes, divided amongst the two groups of physicians:**

To medical officers:	To civilian physicians:
1 $2,000 War Bond (E or F series)	1 $2,000 War Bond (E or F series)
10 $1,000 War Bonds (E or F series)	10 $1,000 War Bonds (E or F series)
10 $ 500 War Bonds (E or F series)	10 $ 500 War Bonds (E or F series)

No physician may submit more than one piece nor win more than one of the 42 prizes. No physician is eligible for a prize unless he also submits for exhibition at either the 1945 or the 1946 annual exhibition of the A.P.A.A. at least one other original work (not previously exhibited at an A.P.A.A. Exhibition) in any medium, on any subject of his own choice. Prizes will be awarded on a basis of conception and execution, irrespective of medium employed.

6. **JUDGES — See Footnote ★**

7. **EXPIRATION DATE — See Footnote ★**

8. **PURPOSE OF THE COMPETITION:** To memorialize the heroism and devotion of the medical profession in war and peace. All exhibitors (including prize-winners) shall retain ownership of their pieces. It is understood, however, that the A.P.A.A. shall have reproduction rights and also the privilege, for a period of three years after the close of the contest, of displaying prize-winning objects, at art museums, libraries, county medical societies, medical schools, hospitals, and similar institutions for the purpose of enhancing the public's estimate of the medical profession. The Association shall also have the right to offer institutions such as those mentioned above, the privilege of copying any of the prize-winning objects for use as murals, cornerstones, friezes, architectural designs, etc. — for the purpose of memorializing the medical profession's importance in war and in peace.

★ **FURTHER INFORMATION** available on request of the Association's Secretary, Dr. F. H. Redewill, Flood Bldg., San Francisco, Cal., or Mead Johnson & Co., Evansville 21, Ind., U.S.A.